

REMARKS

The holding of allowable subject matter in claims 19 and 20 is gratefully acknowledged. Claim 19 has been amended to put it in independent form.

Applicants have narrowed claims in this application. Applicants are not conceding in this application that those claims are not patentable over the art cited by the Examiner, as the present claim amendments and cancellations are only for facilitating expeditious prosecution of the allowable subject matter noted by the examiner. Applicants respectfully reserve the right to pursue these and other claims in one or more continuations and/or divisional patent applications – particularly with respect to non-elected subject matter and other dependent claims.

Formal matters

The objection under rule 37 CFR 1.75(c) is respectfully objected to, because it is impossible to determine which claims are targeted. For instance, claim 11 is mentioned, but it is not multiply dependent. Applicants have tried to fix the problem here, but clarification is respectfully requested.

Also, it is not at all clear why claims 10, 12 and 13 are treated differently in terms of the election requirement from claims 14-16.

Art rejections

The art rejections are respectfully traversed.

Since the references are many and complex, Applicants will confine their remarks to those portions of the references cited by the Examiner, except as otherwise indicated. Applicants make no representation as to the contents of other portions of the references.

REMARKS

Any of the Examiner's rejections and/or points of argument that are not addressed below would appear to be moot in view of the following. Nevertheless, Applicants reserve the right to respond to those rejections and arguments and to advance additional arguments at a later date. No arguments are waived and none of the Examiner's statements are conceded.

Baaten/Nakai rejections

Claim 1

Applicants respectfully submit that the Examiner interprets the language of this claim in a manner that is outside its broadest reasonable scope. The claim recites a first portion of the discharge vessel that is provided with a first electrode and a second portion of the discharge vessel that is provided with a second electrode. The preferred embodiment — shown in Fig. 1 — shows distinct cylindrical portions 11 and 21, each with their own electrodes 12 and 22.

With respect to the primary reference, Baaten, the Examiner points to two portions that are at 180° to each other within a single cylindrical body, per directions A and B on the figures. The body does have two electrodes 2 and 3, but neither can be said to be more associated with one portion or the other portion, they are each equally associated with both portions. The reading of the Examiner that attempts to allocate one electrode to one portion and the other electrode to the other portion is twisting the language of the claims and the reference both out of their ordinary meaning.

Nevertheless, Applicants have added new claim 26, which more clearly states that the first portion surrounds the first electrode and the second portion surrounds the second electrode.

REMARKS

The Examiner cites Nakai for having direct current; however Nakai is a lamp with more than two electrodes. It is therefore not at all clear to one of ordinary skill in the art how to translate the teachings of that reference into the context of Baaten, which has only two electrodes.

Moreover, Nakai seems to have an entirely separate tubular envelope for each color, and specifically seems to teach away in its background section from the concept of using one discharge vessel with different luminescent materials for generating multiple colors. Accordingly, one of ordinary skill in the art would not combine Nakai with Baaten absent impermissible hindsight in light of the Applicants' disclosure and claims.

Claim 10

In rejecting this claim, the Examiner seems to confuse the term

“melanin”

with the term

“melatonin.”

Please note that, despite the similarity in the way they look and sound, these are different words that refer to different substances in the body. The former is a skin pigment. The latter is a hormone that influences sleep, and may help prevent some cancers. The present application relates to melatonin NOT melanin.

Ultra violet radiation, e.g. UV-A, UV-B, per Baaten, influences melanin production. It is not clear that UV particularly influences melatonin production. The present application does not relate to getting a suntan, unlike Baaten. The present application relates to sleeping or drowsiness or lack of alertness.

REMARKS

UV is radiation of wavelength less than 380nm. The wavelengths cited in the application for melatonin suppression are in the visible spectrum, see e.g. p.8, lines 14 et seq. of the specification. In other words, blue visible light tends to suppress melatonin production, while light that is longer wavelength, i.e. redder, tends to allow melatonin production.³

Articles from Wikipedia relating to melanin, melatonin, the visible spectrum, and ultraviolet radiation are appended hereto to further clarify these issues.

Applicants accordingly respectfully submit that Baaten fails to teach or suggest anything relating to melatonin suppression.

Claims 12 & 13

Again, with respect to these claims, the Examiner seems to confuse melanin and melatonin. Reconsideration is accordingly respectfully requested.

Meyer/Nakai

The translation of Meyer is respectfully objected to. The translation translates some terminology in a fashion that is incomprehensible, because the words and sentence order often do not make sense. Moreover, the translation leaves a number of German words untranslated. The meaning of the reference is not clearly apparent.

In any case, as best as Applicants can tell, they believe that Meyer fails to teach or suggest the control means as recited in the amended claim. Reconsideration is accordingly respectfully requested.

Moreover, Nakai seems to have an entirely separate tubular envelope for each color, and specifically seems to teach away in its background section from the concept of using one

REMARKS

discharge vessel with different luminescent materials for generating multiple colors. Accordingly, one of ordinary skill in the art would not combine Nakai with Meyer absent impermissible hindsight in light of the Applicants' disclosure and claims.

Section 3 of the Office Action

This section cites WO 01/15201. Applicants are confused by this citation. This document does not seem to relate to the invention at all and does not seem to appear on the lists of documents of record that are attached to the Office action.

Applicants suppose that the Examiner means to cite WO 01/15204, which is listed as of record – but then the Examiner refers to the document as “De Putter,” who is only the last listed inventor on the document. It is customary to refer to a document by the first listed inventor, who in this case would be van den Bogert.

Clarification as to which reference is intended is accordingly respectfully requested.

Applicants are going to assume that the rejection is intended to refer to WO01/15204 A1. This reference is not believed to be pertinent as Applicants are unable to discern where it might relate to a lamp that has more than one range of spectrum of emitted light. Applicants therefore respectfully submit that one of ordinary skill in the art would not combine it as the Examiner does absent impermissible hindsight in light of Applicants' disclosure.

With respect to claim 3, Applicants do not understand how the amalgam in the reference can be said to teach or suggest a location between the two portions. So far as Applicants can discern, based on the rejection, the amalgam in the reference is in the region of an electrode, not between the two portions.

REMARKS

With respect to claim 4, Applicants do not understand how the reference could be said to teach or suggest an amalgam in the region of an electrode of lower color temperature. So far as Applicants can discern, based on the rejection, neither electrode is associated with a lower color temperature — and in fact the entire lamp is of a single color temperature.

Claim 6 has been amended to incorporate the subject matter of claim 1, without the amalgam, since the specification teaches that the cold spot can be to improve speed of achieving desired color. Applicants respectfully submit that since there is no color control in “De Putter” the reference fails to teach or suggest that a cold spot could be used for this purpose.

Claim 8 recites that the amalgam is provided at the cold spot. The Examiner purports to find this in De Putter. Applicants respectfully disagree. Element 27 is not located at a cold spot. It is right next to the electrode. One of ordinary skill in the art would certainly not understand the reference the way the Examiner interprets it here. Applicants respectfully submit that this is an improper hindsight reconstruction in light of Applicants disclosure and claims.

Baaten/Nakai/Jennato⁴

Claim 18 recites an alternating current, but it also depends from claims that recite a direct current. In other words, the lamp of claim 18 has BOTH alternating and direct currents. As explained in the specification, the direct current is used for color control — even in the presence of alternating current to run the lamp.

In making this rejection, the Examiner cites a portion of Jennato that indicates that either alternating or direct current may be used. Applicants are not seeing that this portion teaches or suggests that both may be used. Applicants accordingly respectfully submit that the Examiner has failed to make a *prima facie* case against claim 18.

REMARKS

Other claim amendments

Claim 2 has been cancelled as redundant with amended claim 1. Other dependent claims have been amended to reflect the cancellation of claim 2.

The amalgam is now introduced in claim 8 again, since claim 6 has been made independent.

INFORMATION DISCLOSURE

The following documents were applied against the claims in Europe in at least one ex-USA office action, and do not appear to be of record:

- WO 99/21214A1
- GB821,668

Please charge any fees other than the issue fee to deposit account 14-1270. Please credit any overpayments to the same account.

REMARKS

Applicants respectfully submit that they have addressed each issue raised by the Examiner — except for any that were skipped as moot — and that the application is accordingly in condition for allowance. Allowance is therefore respectfully requested.

Respectfully submitted,

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REMARKS

¹ In this and subsequent claims, the subscript notation and symbols, which were written out in the previous amendment, have been returned to their original form.

² The paragraph structure of the original claim has been returned in claims 19 and 21.

³ The undersigned has personally changed all the colors on her Windows color scheme on her computer to shades of rose, rather than white, blue or grey, precisely to prevent suppression of melatonin.

⁴ The Examiner has misspelled this name as Jennado.

Melanin

From Wikipedia, the free encyclopedia

Jump to: [navigation](#), [search](#)

Broadly, **melanin** is any of the [polyacetylene](#), [polyaniline](#), and [polypyrrole](#) "blacks" and "browns" or their mixed [copolymers](#). The most common form of [biological melanin](#) is a [polymer](#) of either or both of two [monomer molecules](#): indolequinone, and dihydroxyindole carboxylic acid. Melanin exists in the [plant](#), [animal](#) and [protista kingdoms](#), where it serves as a [pigment](#). The presence of melanin in the [archaea](#) and [bacteria](#) kingdoms is an issue of ongoing debate amongst researchers in the field.

Contents

- [1 Melanin in humans](#)
- [2 Melanin in other organisms](#)
- [3 Synthetic pathways](#)
- [4 Melanin deficiency in genetic disorders and disease states](#)
 - [4.1 Melanin and human adaptation](#)
- [5 Physical properties and technological applications](#)
- [6 Melanin-based bias in human societies](#)
- [7 See also](#)
- [8 References](#)
- [9 External links](#)

[edit] Melanin in humans

In humans, melanin is found in [skin](#), [hair](#), the pigmented tissue underlying the [iris](#), the [medulla](#) and [zona reticularis](#) of the [adrenal gland](#), the [stria vascularis](#) of the [inner ear](#), and in pigment bearing neurons of certain deep brain nuclei such as the [locus ceruleus](#) and the [substantia nigra](#). Melanin is the primary determinant of [human skin color](#).

Dermal melanin is produced by [melanocytes](#), which are found in the [stratum basale](#) of the [epidermis](#). Although human beings generally possess a similar concentration of melanocytes in their skin, the melanocytes in some individuals and ethnic groups more frequently or less frequently [express](#) the melanin-producing [genes](#), thereby conferring a greater or lesser concentration of skin melanin. Some individual animals and humans have very little or no melanin in their bodies, a condition known as [albinism](#).

Because melanin is an aggregate of smaller component molecules, there are a number of different types of melanin with differing proportions and bonding patterns of these component molecules. Both pheomelanin and eumelanin are found in human skin and

hair, but eumelanin is the most abundant melanin in humans, as well as the form most likely to be deficient in albinism.

Eumelanin polymers have long been thought to comprise numerous cross-linked 5,6-dihydroxyindole (DHI) and 5,6-dihydroxyindole-2-carboxylic acid (DHICA) polymers; recent research into the electrical properties of eumelanin, however, has indicated that it may consist of more basic oligomers adhering to one another by some other mechanism. Thus, the precise nature of eumelanin's molecular structure is once again the object of study. ^[citation needed] Eumelanin is found in hair and skin, and colors hair grey, black, yellow, and brown. In humans, it is more abundant in peoples with dark skin. There are two different types of eumelanin, which are distinguished from each other by their pattern of polymer bonds. The two types are black eumelanin and brown eumelanin. Black eumelanin is the darkest, brown eumelanin is lighter than black eumelanin. black eumelanin is in mostly non-Europeans and aged Europeans, while brown eumelanin is in mostly young Europeans. A small amount of black eumelanin in the absence of other pigments causes grey hair. A small amount of brown eumelanin in the absence of other pigments causes yellow (blond) color hair.

Pheomelanin is also found in hair and skin and is both in lighter skinned humans and darker skinned humans. But in general women have more pheomelanin than men, and thus women's skin is generally redder than men's. Pheomelanin imparts a pink to red hue and, thus, is found in particularly large quantities in red hair. Pheomelanin is particularly concentrated in the lips, nipples, glans of the penis, and vagina. Pheomelanin also may become carcinogenic when exposed to the ultraviolet rays of the sun. Chemically, pheomelanin differs from eumelanin in that its oligomer structure incorporates the amino acid L-cysteine, as well as DHI and DHICA units.

Neuromelanin is the dark pigment present in pigment bearing neurons of four deep brain nuclei: the substantia nigra (in Latin, literally "black substance") - Pars Compacta part, the locus ceruleus ("blue spot"), the dorsal motor nucleus of the vagus nerve (cranial nerve X), and the median raphe nucleus of the pons. Both the substantia nigra and locus ceruleus can be easily identified grossly at the time of autopsy due to their dark pigmentation. In humans, these nuclei are not pigmented at the time of birth, but develop pigmentation during maturation to adulthood. Although the functional nature of neuromelanin is unknown in the brain, it may be a byproduct of the synthesis of monoamine neurotransmitters for which the pigmented neurons are the only source. The loss of pigmented neurons from specific nuclei is seen in a variety of neurodegenerative diseases. In Parkinson's disease there is massive loss of dopamine producing pigmented neurons in the substantia nigra. A common finding in advanced Alzheimer's disease is almost complete loss of the norepinephrine producing pigmented neurons of the locus ceruleus. Neuromelanin has been detected in primates and in carnivores such as cats and dogs.

[edit] Melanin in other organisms

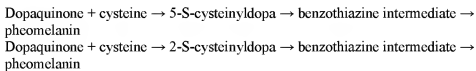
Melanins have very diverse roles and functions in various organisms. They can protect microorganism, such as bacteria and fungi, against stresses that involve cell damage by solar UV radiation or generation of reactive oxygen species. These include high temperature as well as chemical (e.g. heavy metals and oxidizing agents), and biochemical (e.g., host defenses against invading microbes) stresses.^[1] Therefore, in many pathogenic microbes (for example, in *Cryptococcus neoformans*) melanins appear to play important roles in virulence and pathogenicity by protecting the microbe against immune responses of its host. A potentially novel role of melanin as a photosynthetic pigment in some fungi, enabling them to capture gamma rays^[2] and harness its energy for growth has recently been described.^[3] (See radiotrophic fungus) In invertebrates, a major aspect of the innate immune defense system against invading pathogens involves melanin. Within minutes after infection, the microbe is encapsulated within melanin (melanization), and the generation of free radical byproducts during the formation of this capsule is thought to aid in their killing.^[4]

[edit] Synthetic pathways

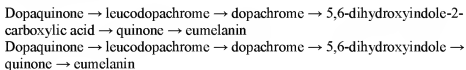
The first step of the synthetic pathway for both eumelanins and pheomelanins is mediated by tyrosinase:



Dopaquinone can combine with cysteine by two pathways to benzothiazines and pheomelanins



Alternatively, dopaquinone can be converted to leucodopachrome and follow two more pathways to the eumelanins



Microscopic appearance

Under the microscope melanin is brown, non-refractile and finely granular with individual granules having a diameter of less than 800 nanometers. This differentiates melanin from common blood breakdown pigments which are larger, chunky and refractile and range in color from green to yellow or red-brown. In heavily pigmented lesions, dense aggregates of melanin can obscure histologic detail. A dilute solution of potassium permanganate is an effective melanin bleach.

[edit] Melanin deficiency in genetic disorders and disease states

Melanin deficiency has been connected for some time with various genetic abnormalities and disease states.

There are approximately ten different types of oculocutaneous albinism, which is mostly an autosomal recessive disorder. Certain ethnicities have higher incidences of different forms. For example, the most common type, called oculocutaneous albinism type 2 (OCA2), is especially frequent among people of black African descent. It is an autosomal recessive disorder characterized by a congenital reduction or absence of melanin pigment in the skin, hair and eyes. The estimated frequency of OCA2 among African-Americans is 1 in 10,000, which contrasts with a frequency of 1 in 36,000 in white Americans^[5]. In some African nations, the frequency of the disorder is even higher, ranging from 1 in 2,000 to 1 in 5,000.^[6] Another form of Albinism, the "yellow oculocutaneous albinism", appears to be more prevalent among the Amish, who are of primarily Swiss and German ancestry. People with this IB variant of the disorder commonly have white hair and skin at birth, but rapidly develop normal skin pigmentation in infancy.^[6]

Ocular albinism affects not only eye pigmentation, but visual acuity, as well. People with albinism typically test poorly, within the 20/60 to 20/400 range. Additionally, two forms of albinism, with approximately 1 in 2700 most prevalent among people of Puerto Rican origin, are associated with mortality beyond melanoma-related deaths.

Mortality also is increased in patients with Hermansky-Pudlak syndrome and Chediak-Higashi syndrome. Patients with Hermansky-Pudlak syndrome have a bleeding diathesis secondary to platelet dysfunction and also experience restrictive lung disease (pulmonary fibrosis), inflammatory bowel disease, cardiomyopathy, and renal disease. Patients with Chediak-Higashi syndrome are susceptible to infection and also can develop lymphofollicular malignancy.^[6]

The role that melanin deficiency plays in such disorders remains under study.

The connection between albinism and deafness has been well known, though poorly understood, for more than a century-and-a-half. In his 1859 treatise *On the Origin of Species*, Charles Darwin observed that "cats which are entirely white and have blue eyes are generally deaf"^[7]. In humans, hypopigmentation and deafness occur together in the rare Waardenburg's syndrome, predominantly observed among the Hopi in North America.^[8] The incidence of albinism in Hopi Indians has been estimated as approximately 1 in 200 individuals. Interestingly, similar patterns of albinism and deafness have been found in other mammals, including dogs and rodents. However, a lack of melanin *per se* does not appear to be directly responsible for deafness associated with hypopigmentation, as most individuals lacking the enzymes required to synthesize melanin have normal auditory function^[9]. Instead the absence of melanocytes in the stria

vascularis of the inner ear results in cochlear impairment^[10], though why this is is not fully understood. It may be that melanin, the best sound absorbing material known, plays some protective function. Alternately, melanin may affect development, as Darwin suggests.

In Parkinson's disease, a disorder that affects neuromotor functioning, there is decreased neuromelanin in the substantia nigra as consequence of specific dropping out of dopaminergic pigmented neurons. This results in diminished dopamine synthesis. While no correlation between race and the level of neuromelanin in the substantia nigra has been reported, the significantly lower incidence of Parkinson's in blacks than in whites has "prompt[ed] some to suggest that cutaneous melanin might somehow serve to protect the neuromelanin in substantia nigra from external toxins."^[11] Also see Nicolaus^[12] review article on the function of neuromelanins

In addition to melanin deficiency, the molecular weight of the melanin polymer may be decreased due to various factors such as oxidative stress, exposure to light, perturbation in its association with melanosomal matrix proteins, changes in pH or in local concentrations of metal ions. A decreased molecular weight or a decrease in the degree of polymerization of ocular melanin has been proposed to turn the normally anti-oxidant polymer into a pro-oxidant. In its pro-oxidant state, melanin has been suggested to be involved in the causation and progression of macular degeneration and melanoma. (Ref: Pigment cell Res. 2001; volume 14: pages 148-154. "Redox regulation in human melanocytes and melanoma")

[edit] Melanin and human adaptation

Melanocytes insert granules of melanin into specialized cellular vesicles called melanosomes. These are then transferred into the other skin cells of the human epidermis. The melanosomes in each recipient cell accumulate atop the cell nucleus, where they protect the nuclear DNA from mutations caused by the ionizing radiation of the sun's ultraviolet rays. People whose ancestors lived for long periods in the regions of the globe near the equator generally have larger quantities of cumelanin in their skins. This makes their skins brown or black and protects them against high levels of exposure to the sun, which more frequently results in melanomas in lighter skinned people.

With humans, exposure to sunlight stimulates the skin to produce vitamin D. Because high levels of cutaneous melanin act as a natural sun screen, dark skin can be a risk factor for vitamin D deficiency.

In Scotland, which lies at a northern latitude, descendants of the Britons have white skin. When their skin is exposed to the meager sunlight, the scant amount of melanin their skin produces is unable to block the sunlight. Therefore, their bodies are able to make Vitamin D with the help of sunlight. Vitamin D, a vitamin found in fish oil, is necessary to prevent rickets, a bone disease caused by too little calcium.

In contrast, in Africa, which is near the equator, humans require intense sunlight to penetrate their dark skin to make Vitamin D. This is all well and good. However, when blacks lived in England during the Industrial Revolution, they were the first to develop symptoms of rickets, such as retarded growth, bowed legs and fractures because not enough sunlight was available.

Fortunately, in 1930, Vitamin D was discovered and dispensed as a supplement to add to the diet. Now many common foods like milk and bread are Vitamin D fortified.

The most recent scientific evidence indicates that all humanity originated in Africa. It is most likely that the first people had relatively large numbers of eumelanin producing melanocytes and, accordingly, darker skin (as displayed by the indigenous people of Africa, today). As some of these original peoples migrated and settled in areas of Asia and Europe, the selective pressure for eumelanin production decreased in climates where radiation from the sun was less intense. Thus variations in genes involved in melanin production began to appear in the population, resulting in lighter hair and skin in humans residing at northern latitudes. Studies have been carried out to determine whether these changes were due to genetic drift or positive selection, perhaps driven by requirement for vitamin D. Of the two common gene variants known to be associated with pale human skin, MC1R^[13] does not appear to have undergone positive selection, while SLC24A5^[14] has.

As with peoples who migrated northward, those with light skin who migrate southward acclimatize to the much stronger solar radiation. Most people's skin darkens when exposed to UV light, giving them more protection when it is needed. This is the physiological purpose of sun tanning. Dark-skinned people, who produce more skin-protecting eumelanin, are less likely to suffer from sunburn and the development of melanoma, a potentially deadly form of skin cancer, as well as other health problems related to exposure to strong solar radiation, including the photodegradation of certain vitamins such as riboflavins, carotenoids, tocopherol, and folate.

Higher eumelanin levels also can be a disadvantage, however, beyond a higher disposition toward vitamin D deficiency. Dark skin is a complicating factor in the laser removal of port-wine stains. Effective in treating white skin, lasers generally are less successful in removing port-wine stains in Asians and people of African descent. Higher concentrations of melanin in darker-skinned individuals simply diffuse and absorb the laser radiation, inhibiting light absorption by the targeted tissue. Melanin similarly can complicate laser treatment of other dermatological conditions in people with darker skin.

Freckles and moles are formed where there is a localized concentration of melanin in the skin. They are highly associated with pale skin.

Melanin in the eyes helps protect them from ultraviolet and high frequency visible light; people with blue eyes are more at risk for sun-related eye problems. Further, the ocular

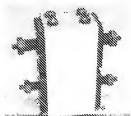
lens yellows with age, providing added protection. However, the lens also becomes more rigid with age, losing most of its accommodation — the ability to change shape to focus from far to near — a detriment due probably to protein crosslinking caused by UV exposure.

Recent research by J.D. Simon *et al.* (Pigment Cell Research, 2004, 17: 262-269) suggests that melanin may serve a protective role other than photoprotection. Melanin is able to effectively ligate metal ions through its carboxylate and phenolic hydroxyl groups, in many cases much more efficiently than the powerful chelating ligand ethylenediaminetetraacetate (EDTA). It may thus serve to sequester potentially toxic metal ions, protecting the rest of the cell. This hypothesis is supported by the fact that the loss of neuromelanin observed in Parkinson's disease is accompanied by an increase in iron levels in the brain.

[edit] Physical properties and technological applications

Melanin is a biopolymer and a neuropeptide^[*citation needed*]. Melanins are "rigid-backbone" conductive polymers composed of polyacetylene, polypyrrole, and polyaniline "Blacks" and their mixed copolymers. The simplest melanin is polyacetylene, from which all others derive^[*citation needed*]. Some fungal melanins are pure polyacetylene.

In 1963, DE Weiss and coworkers reported [1] high electrical conductivity in a melanin, iodine-doped and oxidized polypyrrole "Black". They achieved the quite high conductivity of 1 Ohm/cm. A decade later, John McGinness, and coworkers reported a high conductivity "ON" state in a voltage-controlled solid-state threshold switch made with DOPA melanin [2]. Further, this material emitted a flash of light—electroluminescence—when it switched. Melanin also shows negative resistance, a classic property of electronically-active conductive polymers. Likewise, melanin is the best sound-absorbing material known [15] due to strong electron-phonon coupling. This may be related to melanin's presence in the inner ear.



Melanin voltage-controlled switch, an "active" organic polymer electronic device from 1974. Now in the Smithsonian.

These early discoveries were "lost" until the recent emergence of such melanins in device applications, particularly electroluminescent displays. In 2000, the Nobel Prize in Chemistry was awarded to three scientists for their subsequent 1977 (re)discovery and development of such conductive organic polymers. In an essential reprise of Weiss *et al's* work, these polymers were oxidized, iodine-doped "polyacetylene black" melanins. There

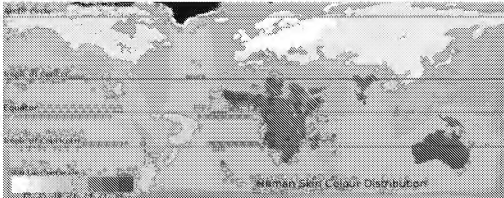
is no evidence the Nobel committee was aware of Weiss *et al*s [3] almost identical prior report of passive high conductivity in iodinated polypyrrole black or of switching and high electrical conductivity in DOPA melanin and related organic semiconductors. The melanin organic electronic device is now in the Smithsonian Institution's National Museum of American History's "Smithsonian Chips" collection of historic solid-state electronic devices.


Melanin influences neural activity and mediates the conduction of radiation, light, heat and kinetic energy. As such, it is the subject of intense interest in biotech research and development, most notably in organic electronics (sometimes called "plastic electronics") and nanotechnology, where dopants are used to dramatically boost melanin conductivity. Pyrrole black and acetylene black are the most commonly studied organic semiconductors.

Although synthetic melanin (commonly referred to as BSM, or "black synthetic matter") is made up of 3-6 oligomeric units linked together—the so-called "protomolecule"—there is no evidence that naturally occurring biopolymer (BCM, for "black cell matter") mimics this structure. However, since there is no reason to believe that natural melanin does not belong to the category of the polyarenes and polycationic polyenes, like pyrrole black and acetylene black, it is necessary to review all the chemical and biological analytic data gathered to date in the study of natural melanins (eumelanins, pheomelanins, allomelanins)." [4]

Evidence exists in support of a highly cross-linked heteropolymer bound covalently to matrix scaffolding melanoproteins (Eur. J. Biochem. 1995; 232: 159-164 "Interaction of melanosomal proteins with melanin). It has been proposed that the ability of melanin to act as an antioxidant is directly proportional to its degree of polymerization or molecular weight (Ophthalmic research, 2005, 37: 136-141 "Melanin aggregation and polymerization: possible implications in age related macular degeneration"). Suboptimal conditions for the effective polymerization of melanin monomers may lead to formation of lower-molecular-weight, pro-oxidant melanin that has been implicated in the causation and progression of macular degeneration and melanoma. (Clinical Cancer Res. 2004; 10: 2581-2583 "Etiologic pathogenesis of melanoma: a unifying hypothesis for the missing attributable risk"). Signaling pathways that upregulate melanization in the retinal pigment epithelium (RPE) also may be implicated in the downregulation of rod outer segment phagocytosis by the RPE. This phenomenon has been attributed in part to foveal sparing in macular degeneration. (Mol. Vis. 2005; 11: 482-490 "Melanization and phagocytosis: implications for age-related macular degeneration).

[edit] Melanin-based bias in human societies



 Human skin color map. Data for native populations collected by R. Biasutti prior to 1940. Consequently, sampling in much of Asia and some remote localities is insufficient (see e.g. Japanese, Inuit and Tibetans which ought to be darker-skinned than represented here because mountain area).

When skin pigmentation as a characteristic of race is linked to social status or other human attributes, this phenomenon is known as racism. Many people and societies overlay racism with racist perceptions and systems which arbitrarily assign to groups of people a status of inherent superiority or inferiority, privilege or disadvantage based on skin color or racial classification. Apartheid-era South Africa is an example of a white supremacist society based on a system of stratification of power and privilege by skin color, as well as racial admixture. Similar examples can be found in India's caste system; Brazil's highly socially color-stratified society; and, in the U.S., segregation and institutional racism on the part of white-controlled institutions, and internal "color consciousness" on the part of members of some ethnic minorities. Because of the pervasive influence of white supremacist values worldwide, prejudice against people with more highly pigmented skin is the most pervasive form of color bias. Conversely, black supremacy is a far less pervasive phenomenon. Many other societies remain informally divided on the basis of skin color and, often, related ethnicity. (See also colonialism, Nazism and institutional racism.)

Illogical presumptions about people with regard to hair color are far less common than skin-color bias, have far fewer and less serious real-world implications, and are more often applied to women than to men. Common stereotypes in the West are dumb blondes, hot-tempered redheads and vixen brunettes.

[edit] See also

- Carotene
- Human skin color
- SLC24A5
- Mc1r
- Melanism

- Melanoma
- Organic semiconductor
- Parkinson's disease
- Racism
- Red hair
- Vitamin D
- Albino
- Griselli syndrome A syndrome characterised by hypopigmentation.

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[edit] External links

- [Absorption spectrum of melanin](#)

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Views

- [Article](#)
- [Discussion](#)
- [Edit this page](#)
- [History](#)

Personal tools

- [Sign in / create account](#)

Navigation

- [Main Page](#)
- [Contents](#)
- [Featured content](#)
- [Current events](#)
- [Random article](#)

interaction

- [About Wikipedia](#)
- [Community portal](#)
- [Recent changes](#)
- [Contact Wikipedia](#)
- [Donate to Wikipedia](#)

- [Help](#)

Search

| | | |
|--|----|--------|
| | Go | Search |
|--|----|--------|

Toolbox

- [What links here](#)
- [Related changes](#)
- [Upload file](#)
- [Special pages](#)
- [Printable version](#)
- [Permanent link](#)
- [Cite this page](#)

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- [Български](#)
- [Deutsch](#)
- [Español](#)
- [Français](#)
- [Italiano](#)
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Melatonin

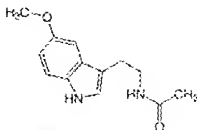
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Jump to: [navigation](#), [search](#)

Melatonin, 5-methoxy-N-acetyltryptamine, is a hormone found in all living creatures from algae^[1] to humans, at levels that vary in a daily cycle.

Many biological effects of melatonin are produced through activation of melatonin receptors,^[2] while others are due to its role as a pervasive and extremely powerful antioxidant^[3] with a particular role in the protection of nuclear and mitochondrial DNA.^[4]

Products containing either or both of isolated or synthesized melatonin have been available as a health supplement in the United States^[5] starting in 1993, and met with good consumer acceptance and enthusiasm.^[6] However, over-the-counter sales remain illegal in many other countries including the members of the European Union, Australia, and New Zealand.^[7]



Melatonin

Systematic (IUPAC) name

N-[2-(5-methoxy-1*H*-indol-3-yl)ethyl]ethanamide

Identifiers

CAS number 73-31-4
ATC code N05CM17
PubChem 896
DrugBank APRD00742

Chemical data

Formula **C₁₃H₁₆N₂O₂**
Mol. mass 232.278 g/mol

Pharmacokinetic data

Bioavailability 30 – 50%
Metabolism Hepatic via CYP1A2 mediated 6-hydroxylation
Half life 35 to 50 minutes
Excretion Urine

Therapeutic considerations

Pregnancy cat. ?
Legal status POM(UK)
Routes ?

Contents

- 1 Production
- 2 Distribution
- 3 Roles in the animal kingdom
- 4 Roles in humans
 - 4.1 Biological clock
 - 4.1.1 Light dependence
 - 4.2 Antioxidant
 - 4.3 Immune system
 - 4.4 Dreaming
- 5 Use as medicinal supplement
 - 5.1 Proposed medical indications
 - 5.1.1 Treatment of circadian rhythm disorders
 - 5.1.2 Preventing ischemic damage
 - 5.1.3 Sleep aid
 - 5.1.4 Learning, memory and Alzheimer's
 - 5.1.5 ADHD
 - 5.1.6 Fertility
 - 5.1.7 Headaches
 - 5.1.8 Depression
 - 5.1.9 Other
 - 5.2 Use as a dietary supplement
 - 5.3 Safety of supplementation
- 6 In popular culture
- 7 See also
- 8 References
- 9 External links

[edit] Production

In higher animals, melatonin is produced by pinealocytes in the pineal gland (located in the brain) and also by the retina, lens and GI tract. It is naturally synthesized from the amino acid tryptophan (via synthesis of serotonin) by the enzyme 5-hydroxyindole-O-methyltransferase.

Production of melatonin by the pineal gland is under the influence of the suprachiasmatic nucleus (SCN) of the hypothalamus which receives information from the retina about the daily pattern of light and darkness. Both SCN rhythmicity and melatonin production are affected by non-visual light information traveling not through the optic nerve, but through the recently-identified hypothalamic tract.

The light/dark information reaches the SCN via a subpopulation of inner retinal ganglion cells, which are intrinsically-photosensitive photoreceptor cells, distinct from those involved in the visual system. These cells represent approximately 2% of retinal ganglion cells in humans and express the non-visual photopigment melanopsin (1). The sensitivity of melanopsin fits with that of a vitamin A-based photopigment with a peak sensitivity at

484 nm (blue light) (2). This photoperiod cue entrains the circadian rhythm, and the resultant production of specific “dark” and “light” induced neural and endocrine signals regulates behavioral and physiological circadian rhythms.^[8]

Melatonin may also be produced by a variety of peripheral cells such as bone marrow cells (3,4), lymphocytes and epithelial cells. Usually, the melatonin concentration in these cells is much higher than that found in the blood but it does not seem to be regulated by the photoperiod.^[9]

Melatonin is also synthesized by various plants, such as rice, and ingested melatonin has been shown to be capable of reaching and binding to melatonin binding sites in the brains of mammals.^{[10][11]}

[edit] Distribution

Melatonin produced in the pineal gland acts as an endocrine hormone since it is released into the blood. By contrast, melatonin produced by the retina and the gastrointestinal (GI) tract acts as a paracrine hormone.

[edit] Roles in the animal kingdom

Many animals use the variation in duration and quantity of melatonin production in each day as a seasonal clock.^[12] In seasonal breeders which do not have long gestation periods, and which mate during longer daylight hours, the melatonin signal controls the seasonal variation in their sexual physiology, and similar physiological effects can be induced by exogenous melatonin in animals including mynah birds^[13] and hamsters.^[14] Melatonin can suppress libido by inhibiting secretion of luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the anterior pituitary gland, especially in mammals that have a breeding season when daylight hours are long. The reproduction of long-day breeders is repressed by melatonin and the reproduction of short-day breeders is stimulated by melatonin.

During the night, melatonin regulates leptin, lowering the levels; see Leptin.

Melatonin is also related to the mechanism by which some amphibians and reptiles change the color of their skin.^{[15][16]}

[edit] Roles in humans

[edit] Biological clock

See also: Phase response curve

In humans, melatonin is produced by the pineal gland, a gland about the size of a pea, located in the center of the brain on the dorsal surface of diencephalon. The melatonin

signal forms part of the system that regulates the circadian cycle by chemically causing drowsiness, but it is the central nervous system that controls the daily cycle in most components of the paracrine and endocrine systems^{[17][18]} rather than the melatonin signal (as was once postulated).

[edit] Light dependence

Production of melatonin by the pineal gland is inhibited by light and permitted by darkness. For this reason melatonin has been called "the hormone of darkness" and its onset each evening is called the Dim-Light Melatonin Onset (DLMO). Secretion of melatonin, and its level in the blood, peaks in the middle of the night, and gradually falls during the second half of the night, with normal variations in timing according to an individual's chronotype.

Until recent history, humans in temperate climates were exposed to up to 18 hours of darkness in the winter. In the modern world, artificial lighting reduces this to typically eight hours or less per day all year round. Even low light levels inhibit melatonin production to some extent, but over-illumination can create significant reduction in melatonin production. Since it is principally blue light that suppresses melatonin^[19] wearing glasses that block blue light^[20] in the hours before bedtime may avoid melatonin loss. Use of blue-blocking goggles the last hours before bedtime has also been advised for people who need to adjust to an earlier bedtime, as melatonin promotes sleepiness.

Reduced melatonin production has been proposed as a likely factor in the significantly higher cancer rates in night workers,^[21] and the effect of modern lighting practice on endogenous melatonin has been proposed as a contributory factor to the larger overall incidence of some cancers in the developed world.^[22] As inadequate as blood concentrations may be in brightly lit environments, some scientists now believe that a person's overnight output of melatonin can be further jeopardized each time he or she interrupts his or her sleep and turns on a bright light (suggesting that using a less-bright nightlight would be safer). Others suggest that such short exposures do no harm.^[23]

[edit] Antioxidant

Besides its primary function as synchronizer of the biological clock, melatonin may exert a powerful anti-oxidant activity. In many lower life forms, it serves only this purpose.^[24]

Melatonin is a powerful antioxidant that can easily cross cell membranes and the blood-brain barrier.^[25] Unlike other antioxidants, melatonin does not undergo redox cycling, the ability of a molecule to undergo reduction and oxidation repeatedly. Redox cycling may allow other antioxidants (such as vitamin C) to regain their antioxidant properties. Melatonin, on the other hand, once oxidized, cannot be reduced to its former state because it forms several stable end-products upon reacting with free radicals. Therefore, it has been referred to as a terminal (or suicidal) antioxidant.^[25]

Recent research indicates that the first metabolite of melatonin in the melatonin antioxidant pathway may be N(1)-acetyl-N(2)-formyl-5-methoxykynuramine or AFMK rather than the common, excreted 6-hydroxymelatonin sulfate. AFMK alone is detectable in unicellular organisms and metazoans. A single AFMK molecule can neutralize up to 10 ROS/RNS since many of the products of the reaction/derivatives (including melatonin) are themselves antioxidants, and so on. This capacity to absorb free radicals extends at least to the quaternary metabolites of melatonin, a process referred to as "the free radical scavenging cascade". This is not true of other, conventional antioxidants.^[24]

In animal models, melatonin has been demonstrated to prevent the damage to DNA by some carcinogens, stopping the mechanism by which they cause cancer.^[26]

The antioxidant activity of melatonin may reduce damage caused by some types of Parkinson's disease, may play a role in preventing cardiac arrhythmia and may increase longevity; it has been shown to increase the average life span of mice by 20% in some studies.^{[27][28][29]}

[edit] Immune system

While it is clear that melatonin interacts with the immune system,^{[30][31]} the details of those interactions are unclear. There have been few trials designed to judge the effectiveness of melatonin in disease treatment. Most existing data are based on small, incomplete, clinical trials. Any positive immunological effect is thought to result from melatonin acting on high affinity receptors (MT1 and MT2) expressed in immunocompetent cells. In preclinical studies, melatonin may enhance cytokine production. (Carrillo-Vico A, Reiter RJ, Lardone PJ, Herrera JL, Fernández-Montesinos R, Guerrero JM, Pozo D. The modulatory role of melatonin on immune responsiveness. Curr Opin Investig Drugs. 2006 May;7(5):423-31. Review.) and by doing this counteract acquired immunodeficiencies. Some studies also suggest that melatonin might be useful fighting infectious disease (Maestroni GJ. The immunotherapeutic potential of melatonin. Expert Opin Investig Drugs. 2001 Mar;10(3):467-76. Review.) including viral and bacterial infections. Endogenous melatonin in human lymphocytes has been related to interleukin-2 (IL-2) production and to the expression of IL-2 receptor {{Carrillo-Vico A, Lardone PJ, Fernández-Santos JM, Martín-Lacave I, Calvo JR, Karasek M, Guerrero JM. Human lymphocyte-synthesized melatonin is involved in the regulation of the interleukin-2/interleukin-2 receptor system. }} This suggests that melatonin is involved in the clonal expansion of antigen-stimulated human T lymphocytes. When taken in conjunction with calcium, it is an immunostimulator^[citation needed] and is used as an adjuvant in some clinical protocols^[citation needed], conversely, the increased immune system activity may aggravate autoimmune disorders. In rheumatoid arthritis patients, melatonin production has been found increased when compared to age-matched healthy controls. (Cutolo M, Maestroni GJ. The melatonin-cytokine connection in rheumatoid arthritis. Ann Rheum Dis. 2005 Aug;64(8):1109-11. Review.).

[edit] Dreaming

Many supplemental melatonin users have reported an increase in the vividness or frequency of dreams. Extremely high doses of melatonin (50mg) dramatically increased REM sleep time and dream activity in both narcoleptics and those without narcolepsy.^[32]

Many psychoactive drugs, such as LSD and cocaine, increase melatonin synthesis.^[32] It has been suggested that nonpolar (lipid-soluble) indolic hallucinogenic drugs emulate melatonin activity in the awakened state and that both act on the same areas of the brain.^[32]

It has been suggested that psychotropic drugs be readmitted in the field of scientific inquiry and therapy.^[33] If so, melatonin may be prioritized for research in this reemerging field of psychiatry.^[34]

[edit] Use as medicinal supplement

Exogenous melatonin, usually taken orally, is, together with light therapy, the standard treatment for delayed sleep phase syndrome. It appears to have some use against other circadian rhythm sleep disorders, such as jet lag. It has been studied for the treatment of cancer, immune disorders, cardiovascular diseases, depression, seasonal affective disorder (SAD), and sexual dysfunction. A study by Alfred J. Lewy and other researchers at Oregon Health & Science University found that it may ameliorate SAD and circadian misalignment,^[35] but as of 2006 it is known to affect the timing of endogenous melatonin production during long-term melatonin treatment in rats, raising the risk that it can exacerbate both clinical depression and SAD.^[36] Basic research indicates that melatonin may play a significant role in modulating the effects of drugs of abuse such as cocaine.^[37]

[edit] Proposed medical indications

[edit] Treatment of circadian rhythm disorders

Exogenous melatonin, usually taken orally in the afternoon or evening, is, together with light therapy upon awakening, the standard treatment for delayed sleep phase syndrome and non-24-hour sleep-wake syndrome. See Phase response curve, PRC. It appears to have some use against other circadian rhythm sleep disorders, such as jet lag and the problems of people who work rotating or night shifts.

[edit] Preventing ischemic damage

Melatonin has been shown to reduce tissue damage in rats due to ischemia in both the brain^[38] and the heart,^[39] however, this has not been tested in humans.

[edit] Sleep aid

Melatonin may be used as an adjunct to sleep in children, for certain diagnostic tests.^[40]

[edit] Learning, memory and Alzheimer's

Melatonin receptors appear to be important in mechanisms of learning and memory in mice,^[41] and melatonin can alter electrophysiological processes associated with memory, such as long-term potentiation (LTP). Melatonin has been shown to prevent the hyperphosphorylation of the tau protein in rats. Hyperphosphorylation of tau protein can result in the formation of neurofibrillary tangles, a pathological feature seen in Alzheimer's disease. Thus, melatonin may be effective for treating Alzheimer's Disease.^[42] These same neurofibrillary tangles can be found in the hypothalamus in patients with Alzheimer's, adversely affecting their bodies' production of melatonin. Those Alzheimer's patients with this specific affliction often show heightened afternoon agitation, called *sundowning*, which has been shown in many studies to be effectively treated with melatonin supplements in the evening.^[43]

[edit] ADHD

ADHD is most commonly treated with methylphenidate which may cause insomnia in approximately 94% of its users.^[citation needed] Research shows that after melatonin is administered to the patients, the time needed to fall asleep is significantly reduced. Before the melatonin was administered, the time needed to fall asleep ranged from 15 minutes to 240 minutes. After the melatonin was administered, the time needed to fall asleep ranged from 15 minutes to 64 minutes. Furthermore, the effects of the melatonin after three months showed no change from its effects after one week of use.^[44]

[edit] Fertility

Recent research has concluded that melatonin supplementation in perimenopausal women produces a highly significant improvement in thyroid function and gonadotropin levels, as well as restoring fertility and menstruation and preventing the depression associated with the menopause.^[45]

However, at the same time, some resources warn women trying to conceive not to take a melatonin supplement.^[46]

[edit] Headaches

Several clinical studies indicate that supplementation with melatonin is an effective preventative treatment for migraines and cluster headaches.^{[47][48]}

[edit] Depression

Melatonin has been shown to be effective in treating one form of depression, seasonal affective disorder. [1]

[edit] Other

Some studies have shown that melatonin has potential for use in the treatment of various forms of cancer, HIV, and other viral diseases; however, further testing is necessary to confirm this.^[49]

Histologically speaking, it is also believed that melatonin has some effects for sexual growth in higher organisms. (*Quoted from Ross Histology and Wheather's Functional Histology.)

[edit] Use as a dietary supplement

The primary motivation for the use of melatonin as a supplement is as a natural aid to better sleep, with other incidental benefits to health and well-being due to its role as an antioxidant and its stimulation of the immune system and several components of the endocrine system.

Studies from Massachusetts Institute of Technology say that melatonin pills sold as supplements contain three to ten times the amount needed to produce the desirable physiologic nocturnal blood melatonin level for enhancement of nighttime rest. Dosages are designed to raise melatonin levels for several hours to enhance quality of sleep, but some studies suggest that smaller doses are just as effective at improving sleep quality.^[50] High dose melatonin can even be counterproductive: Lewy & al^[51] provide support to the "idea that too much melatonin may spill over onto the wrong zone of the melatonin phase-response curve." In their study, 0.5 mg of melatonin was effective while 20 mg wasn't. Melatonin supplementation for sleep problems is available without prescription in most cases in the United States and Canada, while it is available only by prescription or not at all in some other countries. Melatonin supplements are available as oral supplements and transdermal melatonin or "melatonin sleep patch".

Melatonin is involved in the regulation of body weight, and may be helpful in treating obesity (especially when combined with calcium).^[52]

[edit] Safety of supplementation



This section has been nominated to be checked for its neutrality.

Discussion of this nomination can be found on the talk page.

Melatonin derived from animal sources may be contaminated with viral material, so synthetic melatonin is generally used to avoid this risk.^[53]

Melatonin is practically nontoxic and exhibits almost no short-term side effects. No studies have as yet been conducted to determine whether there are any long-term side effects. There are, however, case reports about patients who have taken the supplement for years.

Ingesting melatonin supplements may cause some unwanted side effects, especially at high doses (~more than 3 mg/day): hormone fluctuations,[2] irritability,[3] reduced blood flow (see below), and increased sleep disturbances, including vivid nightmares.[4]

Melatonin taken in combination with monoamine oxidase inhibitors (MAOIs) can lead to overdose because MAOIs inhibit the breakdown of melatonin by the body.

Exogenous melatonin normally does not affect the endogenous melatonin profile, merely advancing the phase of endogenous melatonin production in time if taken at an appropriate time of day.

In individuals with auto-immune disorders, there is concern that melatonin supplementation may exacerbate symptoms due to stimulation of the immune system.^[54]

Melatonin causes somnolence, and therefore caution should be shown when driving, operating machinery, etc. When taken several hours before bedtime in accordance with the Phase Response Curve for melatonin in humans, the dosage should be so tiny as to not cause tiredness/sleepiness.

Individuals who experience orthostatic intolerance, a cardiovascular condition that results in reduced blood pressure and blood flow to the brain when a person stands, may experience a worsening of symptoms when taking melatonin supplements, a study at Penn State College of Medicine's Milton S. Hershey Medical Center suggests. Melatonin can exacerbate the symptoms by reducing nerve activity in those who experience the condition, the study found.^[52]

[edit] In popular culture

- Melatonin is the title of a 1998 song by English rock band Radiohead, released as a b-side, and compiled on the album *Airbag/How Am I Driving?*.
- Melatonin is mentioned extensively in William Gibson's 2003 novel *Pattern Recognition*, as the novel deals with jet lag.
- Melatonin is the title of the first track of the Silver Lake-based indie rock band Silversun Pickups' 2006 debut album, *Carnavas*.
- Melatonin is the title of a song by Punk Rock band Smoke or Fire on their album *This Sinking Ship*.

[edit] See also

- Light pollution
- Ramclicon

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[edit] External links

- [MedlinePlus DrugInfo natural-patient-melatonin](#)
- [ASSESSMENT REPORT FOR CIRCADIN[®]](#) by European Medicines Agency (PDF)
- [SUMMARY OF PRODUCT CHARACTERISTICS FOR CIRCADIN[®]](#) by European Medicines Agency (PDF)
- [Melatonin for jet lag?](#). Bandolier #82 (2000), reporting Spitzer et al (1999).
- Herxheimer A, Petrie KJ. Melatonin for the prevention and treatment of jet lag (Cochrane Review). In: *The Cochrane Library*, Issue 2, 2003.
- Do not mail Melatonin to someone in Germany. It is [prohibited](#)

Endocrine system: hormones/endocrine glands (*Peptide hormones, Steroid hormones*)

| | |
|-------------------------------|--|
| Hypothalamic-pituitary | Hypothalamus: TRH, CRH, GnRH, GHRH, somatostatin, dopamine • Posterior pituitary: vasopressin, oxytocin • Anterior pituitary: α (FSH, LH, TSH), GH, prolactin, POMC (ACTH, MSH, endorphins, lipotropin) |
| Adrenal axis | Adrenal medulla: epinephrine, norepinephrine • Adrenal cortex: aldosterone, cortisol, DHEA |
| Thyroid axis | Thyroid: thyroid hormone (T_3 and T_4) • calcitonin • Parathyroid: PTH |
| Gonadal axis | Testis: testosterone, AMH, inhibin • Ovary: estradiol, progesterone, inhibin/activin, relaxin (pregnancy) |
| Other end. glands | Pancreas: glucagon, insulin, somatostatin • Pineal gland: melatonin |
| Non-end. glands | Placenta: hCG, HPL, estrogen, progesterone • Kidney: renin, EPO, calcitriol, prostaglandin • Heart atrium: ANP • Stomach: gastrin, ghrelin • Duodenum: CCK, GLP, secretin, motilin, VIP • Ileum: enteroglucagon • Adipose tissue: leptin, adiponectin, resistin • Thymus: Thymosin • Thymopoietin • Skeleton: Osteocalcin • Liver/other: Insulin-like growth factor (IGF-1, IGF-2) |
| Target-derived | NGF, BDNF, NT-3 |

Dietary supplements

| | |
|---------------------------------|--|
| Types | Amino acids • Bodybuilding supplement • Energy drink • Energy bar • Fatty acids • Herbal Supplements • Minerals • Probiotics • Vitamins • Whole food supplements |
| Vitamins and minerals | Retinol (Vitamin A) • B vitamins: Thiamine (B_1) • Riboflavin (B_2) • Niacin (B_3) • Pantothenic acid (B_5) • Pyridoxine (B_6) • Biotin (B_7) • Folic acid (B_9) • Cyanocobalamin (B_{12}) • Ascorbic acid (Vitamin C) • Ergocalciferol and Cholecalciferol (Vitamin D) • Tocopherol (Vitamin E) • Naphthoquinone (Vitamin K) • Calcium • Choline • Chlorine • Chromium • Cobalt • Copper • Fluorine • Iodine • Iron • Magnesium • Manganese • Molybdenum • Phosphorus • Potassium • Selenium • Sodium • Sulfur • Zinc |
| Other common ingredients | Carnitine • Chondroitin sulfate • Cod liver oil • Copper gluconate • Creatine • Dietary fiber • Elemental calcium • Ephedra • Fish oil • Folic acid • Ginseng • Glucosamine • Glutamine • Iron supplements • Japanese Honeysuckle • Krill oil • Lactobacillus • Lingzhi • Linseed oil • Melatonin • Red yeast rice • Royal jelly • Saw palmetto • Spirulina • Taurine • Wheatgrass • Wolfberry • Yohimbine • Zinc gluconate |

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Tryptamines

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• d • g

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Piperidinedione

Glutethimide • Methypylon • Pyrithyldione

Quinazolinone

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- [Article](#)
- [Discussion](#)
- [Edit this page](#)
- [History](#)

Personal tools

- [Sign in / create account](#)

Navigation

- [Main Page](#)
- [Contents](#)
- [Featured content](#)
- [Current events](#)
- [Random article](#)

interaction

- [About Wikipedia](#)
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- [Upload file](#)
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- [Permanent link](#)
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Melatonin

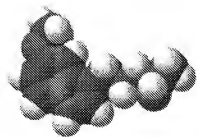
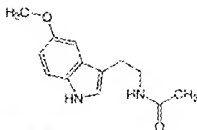
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Melatonin, 5-methoxy-N-acetyltryptamine, is a hormone found in all living creatures from algae^[1] to humans, at levels that vary in a daily cycle.

Many biological effects of melatonin are produced through activation of melatonin receptors,^[2] while others are due to its role as a pervasive and extremely powerful antioxidant^[3] with a particular role in the protection of nuclear and mitochondrial DNA.^[4]

Products containing either or both of isolated or synthesized melatonin have been available as a health supplement in the United States^[5] starting in 1993, and met with good consumer acceptance and enthusiasm.^[6] However, over-the-counter sales remain illegal in many other countries including the members of the European Union, Australia, and New Zealand.^[7]



Melatonin

Systematic (IUPAC) name

N-[2-(5-methoxy-1*H*-indol-3-yl)ethyl]ethanamide

Identifiers

| | |
|------------|-----------|
| CAS number | 73-31-4 |
| ATC code | N05CM17 |
| PubChem | 896 |
| DrugBank | APRD00742 |

Chemical data

| | |
|-----------|---|
| Formula | C ₁₃ H ₁₆ N ₂ O ₂ |
| Mol. mass | 232.278 g/mol |

Pharmacokinetic data

| | |
|-----------------|---|
| Bioavailability | 30 – 50% |
| Metabolism | Hepatic via CYP1A2 mediated 6-hydroxylation |
| Half life | 35 to 50 minutes |
| Excretion | Urine |

Therapeutic considerations

| | |
|----------------|---------|
| Pregnancy cat. | ? |
| Legal status | POM(UK) |
| Routes | ? |

Contents

- 1 Production
- 2 Distribution
- 3 Roles in the animal kingdom
- 4 Roles in humans
 - 4.1 Biological clock
 - 4.1.1 Light dependence
 - 4.2 Antioxidant
 - 4.3 Immune system
 - 4.4 Dreaming
- 5 Use as medicinal supplement
 - 5.1 Proposed medical indications
 - 5.1.1 Treatment of circadian rhythm disorders
 - 5.1.2 Preventing ischemic damage
 - 5.1.3 Sleep aid
 - 5.1.4 Learning, memory and Alzheimer's
 - 5.1.5 ADHD
 - 5.1.6 Fertility
 - 5.1.7 Headaches
 - 5.1.8 Depression
 - 5.1.9 Other
 - 5.2 Use as a dietary supplement
 - 5.3 Safety of supplementation
- 6 In popular culture
- 7 See also
- 8 References
- 9 External links

[edit] Production

In higher animals, melatonin is produced by pinealocytes in the pineal gland (located in the brain) and also by the retina, lens and GI tract. It is naturally synthesized from the amino acid tryptophan (via synthesis of serotonin) by the enzyme 5-hydroxyindole-O-methyltransferase.

Production of melatonin by the pineal gland is under the influence of the suprachiasmatic nucleus (SCN) of the hypothalamus which receives information from the retina about the daily pattern of light and darkness. Both SCN rhythmicity and melatonin production are affected by non-visual light information traveling not through the optic nerve, but through the recently-identified hypothalamic tract.

The light/dark information reaches the SCN via a subpopulation of inner retinal ganglion cells, which are intrinsically-photosensitive photoreceptor cells, distinct from those involved in the visual system. These cells represent approximately 2% of retinal ganglion cells in humans and express the non-visual photopigment melanopsin (1). The sensitivity of melanopsin fits with that of a vitamin A-based photopigment with a peak sensitivity at

484 nm (blue light) (2). This photoperiod cue entrains the circadian rhythm, and the resultant production of specific “dark” and “light” induced neural and endocrine signals regulates behavioral and physiological circadian rhythms.^[8]

Melatonin may also be produced by a variety of peripheral cells such as bone marrow cells (3,4), lymphocytes and epithelial cells. Usually, the melatonin concentration in these cells is much higher than that found in the blood but it does not seem to be regulated by the photoperiod.^[9]

Melatonin is also synthesized by various plants, such as rice, and ingested melatonin has been shown to be capable of reaching and binding to melatonin binding sites in the brains of mammals.^{[10][11]}

[edit] Distribution

Melatonin produced in the pineal gland acts as an endocrine hormone since it is released into the blood. By contrast, melatonin produced by the retina and the gastrointestinal (GI) tract acts as a paracrine hormone.

[edit] Roles in the animal kingdom

Many animals use the variation in duration and quantity of melatonin production in each day as a seasonal clock.^[12] In seasonal breeders which do not have long gestation periods, and which mate during longer daylight hours, the melatonin signal controls the seasonal variation in their sexual physiology, and similar physiological effects can be induced by exogenous melatonin in animals including mynah birds^[13] and hamsters.^[14] Melatonin can suppress libido by inhibiting secretion of luteinizing hormone (LH) and follicle stimulating hormone (FSH) from the anterior pituitary gland, especially in mammals that have a breeding season when daylight hours are long. The reproduction of long-day breeders is repressed by melatonin and the reproduction of short-day breeders is stimulated by melatonin.

During the night, melatonin regulates leptin, lowering the levels; see Leptin.

Melatonin is also related to the mechanism by which some amphibians and reptiles change the color of their skin.^{[15][16]}

[edit] Roles in humans

[edit] Biological clock

See also: Phase response curve

In humans, melatonin is produced by the pineal gland, a gland about the size of a pea, located in the center of the brain on the dorsal surface of diencephalon. The melatonin

signal forms part of the system that regulates the circadian cycle by chemically causing drowsiness, but it is the central nervous system that controls the daily cycle in most components of the paracrine and endocrine systems^{[17][18]} rather than the melatonin signal (as was once postulated).

[edit] Light dependence

Production of melatonin by the pineal gland is inhibited by light and permitted by darkness. For this reason melatonin has been called "the hormone of darkness" and its onset each evening is called the Dim-Light Melatonin Onset (DLMO). Secretion of melatonin, and its level in the blood, peaks in the middle of the night, and gradually falls during the second half of the night, with normal variations in timing according to an individual's chronotype.

Until recent history, humans in temperate climates were exposed to up to 18 hours of darkness in the winter. In the modern world, artificial lighting reduces this to typically eight hours or less per day all year round. Even low light levels inhibit melatonin production to some extent, but over-illumination can create significant reduction in melatonin production. Since it is principally blue light that suppresses melatonin^[19] wearing glasses that block blue light^[20] in the hours before bedtime may avoid melatonin loss. Use of blue-blocking goggles the last hours before bedtime has also been advised for people who need to adjust to an earlier bedtime, as melatonin promotes sleepiness.

Reduced melatonin production has been proposed as a likely factor in the significantly higher cancer rates in night workers,^[21] and the effect of modern lighting practice on endogenous melatonin has been proposed as a contributory factor to the larger overall incidence of some cancers in the developed world.^[22] As inadequate as blood concentrations may be in brightly lit environments, some scientists now believe that a person's overnight output of melatonin can be further jeopardized each time he or she interrupts his or her sleep and turns on a bright light (suggesting that using a less-bright nightlight would be safer). Others suggest that such short exposures do no harm.^[23]

[edit] Antioxidant

Besides its primary function as synchronizer of the biological clock, melatonin may exert a powerful anti-oxidant activity. In many lower life forms, it serves only this purpose.^[24]

Melatonin is a powerful antioxidant that can easily cross cell membranes and the blood-brain barrier.^[25] Unlike other antioxidants, melatonin does not undergo redox cycling, the ability of a molecule to undergo reduction and oxidation repeatedly. Redox cycling may allow other antioxidants (such as vitamin C) to regain their antioxidant properties. Melatonin, on the other hand, once oxidized, cannot be reduced to its former state because it forms several stable end-products upon reacting with free radicals. Therefore, it has been referred to as a terminal (or suicidal) antioxidant.^[25]

Recent research indicates that the first metabolite of melatonin in the melatonin antioxidant pathway may be N(1)-acetyl-N(2)-formyl-5-methoxykynuramine or AFMK rather than the common, excreted 6-hydroxymelatonin sulfate. AFMK alone is detectable in unicellular organisms and metazoans. A single AFMK molecule can neutralize up to 10 ROS/RNS since many of the products of the reaction/derivatives (including melatonin) are themselves antioxidants, and so on. This capacity to absorb free radicals extends at least to the quaternary metabolites of melatonin, a process referred to as "the free radical scavenging cascade". This is not true of other, conventional antioxidants.^[24]

In animal models, melatonin has been demonstrated to prevent the damage to DNA by some carcinogens, stopping the mechanism by which they cause cancer.^[26]

The antioxidant activity of melatonin may reduce damage caused by some types of Parkinson's disease, may play a role in preventing cardiac arrhythmia and may increase longevity; it has been shown to increase the average life span of mice by 20% in some studies.^{[27][28][29]}

[edit] Immune system

While it is clear that melatonin interacts with the immune system,^{[30][31]} the details of those interactions are unclear. There have been few trials designed to judge the effectiveness of melatonin in disease treatment. Most existing data are based on small, incomplete, clinical trials. Any positive immunological effect is thought to result from melatonin acting on high affinity receptors (MT1 and MT2) expressed in immunocompetent cells. In preclinical studies, melatonin may enhance cytokine production. (Carrillo-Vico A, Reiter RJ, Lardone PJ, Herrera JL, Fernández-Montesinos R, Guerrero JM, Pozo D. The modulatory role of melatonin on immune responsiveness. *Curr Opin Investig Drugs*. 2006 May;7(5):423-31. Review.) and by doing this counteract acquired immunodeficiencies. Some studies also suggest that melatonin might be useful fighting infectious disease (Maestroni GJ. The immunotherapeutic potential of melatonin. *Expert Opin Investig Drugs*. 2001 Mar;10(3):467-76. Review.) including viral and bacterial infections. Endogenous melatonin in human lymphocytes has been related to interleukin-2 (IL-2) production and to the expression of IL-2 receptor {{Carrillo-Vico A, Lardone PJ, Fernández-Santos JM, Martín-Lacave I, Calvo JR, Karasek M, Guerrero JM. Human lymphocyte-synthesized melatonin is involved in the regulation of the interleukin-2/interleukin-2 receptor system. }} This suggests that melatonin is involved in the clonal expansion of antigen-stimulated human T lymphocytes. When taken in conjunction with calcium, it is an immunostimulator^[citation needed] and is used as an adjuvant in some clinical protocols^[citation needed], conversely, the increased immune system activity may aggravate autoimmune disorders. In rheumatoid arthritis patients, melatonin production has been found increased when compared to age-matched healthy controls. (Cutolo M, Maestroni GJ. The melatonin-cytokine connection in rheumatoid arthritis. *Ann Rheum Dis*. 2005 Aug;64(8):1109-11. Review.).

[edit] Dreaming

Many supplemental melatonin users have reported an increase in the vividness or frequency of dreams. Extremely high doses of melatonin (50mg) dramatically increased REM sleep time and dream activity in both narcoleptics and those without narcolepsy.^[32]

Many psychoactive drugs, such as LSD and cocaine, increase melatonin synthesis.^[32] It has been suggested that nonpolar (lipid-soluble) indolic hallucinogenic drugs emulate melatonin activity in the awakened state and that both act on the same areas of the brain.^[32]

It has been suggested that psychotropic drugs be readmitted in the field of scientific inquiry and therapy.^[33] If so, melatonin may be prioritized for research in this reemerging field of psychiatry.^[34]

[edit] Use as medicinal supplement

Exogenous melatonin, usually taken orally, is, together with light therapy, the standard treatment for delayed sleep phase syndrome. It appears to have some use against other circadian rhythm sleep disorders, such as jet lag. It has been studied for the treatment of cancer, immune disorders, cardiovascular diseases, depression, seasonal affective disorder (SAD), and sexual dysfunction. A study by Alfred J. Lewy and other researchers at Oregon Health & Science University found that it may ameliorate SAD and circadian misalignment,^[35] but as of 2006 it is known to affect the timing of endogenous melatonin production during long-term melatonin treatment in rats, raising the risk that it can exacerbate both clinical depression and SAD.^[36] Basic research indicates that melatonin may play a significant role in modulating the effects of drugs of abuse such as cocaine.^[37]

[edit] Proposed medical indications

[edit] Treatment of circadian rhythm disorders

Exogenous melatonin, usually taken orally in the afternoon or evening, is, together with light therapy upon awakening, the standard treatment for delayed sleep phase syndrome and non-24-hour sleep-wake syndrome. See Phase response curve, PRC. It appears to have some use against other circadian rhythm sleep disorders, such as jet lag and the problems of people who work rotating or night shifts.

[edit] Preventing ischemic damage

Melatonin has been shown to reduce tissue damage in rats due to ischemia in both the brain^[38] and the heart,^[39] however, this has not been tested in humans.

[edit] Sleep aid

Melatonin may be used as an adjunct to sleep in children, for certain diagnostic tests.^[40]

[edit] Learning, memory and Alzheimer's

Melatonin receptors appear to be important in mechanisms of learning and memory in mice,^[41] and melatonin can alter electrophysiological processes associated with memory, such as long-term potentiation (LTP). Melatonin has been shown to prevent the hyperphosphorylation of the tau protein in rats. Hyperphosphorylation of tau protein can result in the formation of neurofibrillary tangles, a pathological feature seen in Alzheimer's disease. Thus, melatonin may be effective for treating Alzheimer's Disease.^[42] These same neurofibrillary tangles can be found in the hypothalamus in patients with Alzheimer's, adversely affecting their bodies' production of melatonin. Those Alzheimer's patients with this specific affliction often show heightened afternoon agitation, called *sundowning*, which has been shown in many studies to be effectively treated with melatonin supplements in the evening.^[43]

[edit] ADHD

ADHD is most commonly treated with methylphenidate which may cause insomnia in approximately 94% of its users.^[citation needed] Research shows that after melatonin is administered to the patients, the time needed to fall asleep is significantly reduced. Before the melatonin was administered, the time needed to fall asleep ranged from 15 minutes to 240 minutes. After the melatonin was administered, the time needed to fall asleep ranged from 15 minutes to 64 minutes. Furthermore, the effects of the melatonin after three months showed no change from its effects after one week of use.^[44]

[edit] Fertility

Recent research has concluded that melatonin supplementation in perimenopausal women produces a highly significant improvement in thyroid function and gonadotropin levels, as well as restoring fertility and menstruation and preventing the depression associated with the menopause.^[45]

However, at the same time, some resources warn women trying to conceive not to take a melatonin supplement.^[46]

[edit] Headaches

Several clinical studies indicate that supplementation with melatonin is an effective preventative treatment for migraines and cluster headaches.^{[47][48]}

[edit] Depression

Melatonin has been shown to be effective in treating one form of depression, seasonal affective disorder. [1]

[edit] Other

Some studies have shown that melatonin has potential for use in the treatment of various forms of cancer, HIV, and other viral diseases; however, further testing is necessary to confirm this.^[49]

Histologically speaking, it is also believed that melatonin has some effects for sexual growth in higher organisms. (*Quoted from Ross Histology and Wheather's Functional Histology.)

[edit] Use as a dietary supplement

The primary motivation for the use of melatonin as a supplement is as a natural aid to better sleep, with other incidental benefits to health and well-being due to its role as an antioxidant and its stimulation of the immune system and several components of the endocrine system.

Studies from Massachusetts Institute of Technology say that melatonin pills sold as supplements contain three to ten times the amount needed to produce the desirable physiologic nocturnal blood melatonin level for enhancement of nighttime rest. Dosages are designed to raise melatonin levels for several hours to enhance quality of sleep, but some studies suggest that smaller doses are just as effective at improving sleep quality.^[50] High dose melatonin can even be counterproductive: Lewy & al^[51] provide support to the "idea that too much melatonin may spill over onto the wrong zone of the melatonin phase-response curve." In their study, 0.5 mg of melatonin was effective while 20 mg wasn't. Melatonin supplementation for sleep problems is available without prescription in most cases in the United States and Canada, while it is available only by prescription or not at all in some other countries. Melatonin supplements are available as oral supplements and transdermal melatonin or "melatonin sleep patch".

Melatonin is involved in the regulation of body weight, and may be helpful in treating obesity (especially when combined with calcium).^[52]

[edit] Safety of supplementation



This section has been nominated to be checked for its neutrality.

Discussion of this nomination can be found on the talk page.

Melatonin derived from animal sources may be contaminated with viral material, so synthetic melatonin is generally used to avoid this risk.^[53]

Melatonin is practically nontoxic and exhibits almost no short-term side effects. No studies have as yet been conducted to determine whether there are any long-term side effects. There are, however, case reports about patients who have taken the supplement for years.

Ingesting melatonin supplements may cause some unwanted side effects, especially at high doses (~more than 3 mg/day): hormone fluctuations,[2] irritability,[3] reduced blood flow (see below), and increased sleep disturbances, including vivid nightmares.[4]

Melatonin taken in combination with monoamine oxidase inhibitors (MAOIs) can lead to overdose because MAOIs inhibit the breakdown of melatonin by the body.

Exogenous melatonin normally does not affect the endogenous melatonin profile, merely advancing the phase of endogenous melatonin production in time if taken at an appropriate time of day.

In individuals with auto-immune disorders, there is concern that melatonin supplementation may exacerbate symptoms due to stimulation of the immune system.^[54]

Melatonin causes somnolence, and therefore caution should be shown when driving, operating machinery, etc. When taken several hours before bedtime in accordance with the Phase Response Curve for melatonin in humans, the dosage should be so tiny as to not cause tiredness/sleepiness.

Individuals who experience orthostatic intolerance, a cardiovascular condition that results in reduced blood pressure and blood flow to the brain when a person stands, may experience a worsening of symptoms when taking melatonin supplements, a study at Penn State College of Medicine's Milton S. Hershey Medical Center suggests. Melatonin can exacerbate the symptoms by reducing nerve activity in those who experience the condition, the study found.^[52]

[edit] In popular culture

- Melatonin is the title of a 1998 song by English rock band Radiohead, released as a b-side, and compiled on the album *Airbag/How Am I Driving?*.
- Melatonin is mentioned extensively in William Gibson's 2003 novel *Pattern Recognition*, as the novel deals with jet lag.
- Melatonin is the title of the first track of the Silver Lake-based indie rock band Silversun Pickups' 2006 debut album, *Carnavas*.
- Melatonin is the title of a song by Punk Rock band Smoke or Fire on their album *This Sinking Ship*.

[edit] See also

- Light pollution
- Ramclicon

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- [MedlinePlus DrugInfo natural-patient-melatonin](#)
- [ASSESSMENT REPORT FOR CIRCADIN[®]](#) by European Medicines Agency (PDF)
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- [Melatonin for jet lag?](#). Bandolier #82 (2000), reporting Spitzer et al (1999).
- Herxheimer A, Petrie KJ. Melatonin for the prevention and treatment of jet lag (Cochrane Review). In: *The Cochrane Library*, Issue 2, 2003.
- Do not mail Melatonin to someone in Germany. It is [prohibited](#)

Endocrine system: hormones/endocrine glands (*Peptide hormones, Steroid hormones*)

| | |
|------------------------|--|
| Hypothalamic-pituitary | Hypothalamus: TRH, CRH, GnRH, GHRH, somatostatin, dopamine • Posterior pituitary: vasopressin, oxytocin • Anterior pituitary: α (FSH, LH, TSH), GH, prolactin, POMC (ACTH, MSH, endorphins, lipotropin) |
| | Adrenal axis: Adrenal medulla: epinephrine, norepinephrine • Adrenal cortex: aldosterone, cortisol, DHEA |
| Thyroid axis | Thyroid: thyroid hormone (T_3 and T_4) • calcitonin • Parathyroid: PTH |
| Gonadal axis | Testis: testosterone, AMH, inhibin • Ovary: estradiol, progesterone, inhibin/activin, relaxin (pregnancy) |
| Other end. glands | Pancreas: glucagon, insulin, somatostatin • Pineal gland: melatonin |
| Non-end. glands | Placenta: hCG, HPL, estrogen, progesterone • Kidney: renin, EPO, calcitriol, prostaglandin • Heart atrium: ANP • Stomach: gastrin, ghrelin • Duodenum: CCK, GIP, secretin, motilin, VIP • Ileum: enteroglucagon • Adipose tissue: leptin, adiponectin, resistin • Thymus: Thymosin • Thymopoietin • Skeleton: Osteocalcin • Liver/other: Insulin-like growth factor (IGF-1, IGF-2) |
| | Target-derived NGF, BDNF, NT-3 |

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| | |
|--------------------------|--|
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| | Retinol (Vitamin A) • B vitamins: Thiamine (B_1) • Riboflavin (B_2) • Niacin (B_3) • Pantothenic acid (B_5) • Pyridoxine (B_6) • Biotin (B_7) • Folic acid (B_9) • Cyanocobalamin (B_{12}) • Ascorbic acid (Vitamin C) • Ergocalciferol and Cholecalciferol (Vitamin D) • Tocopherol (Vitamin E) • Naphthoquinone (Vitamin K) • Calcium • Choline • Chlorine • Chromium • Cobalt • Copper • Fluorine • Iodine • Iron • Magnesium • Manganese • Molybdenum • Phosphorus • Potassium • Selenium • Sodium • Sulfur • Zinc |
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| Other common ingredients | |

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Benzodiazepine

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Piperidinedione Glutethimide • Methypylon • Pyrithyldione

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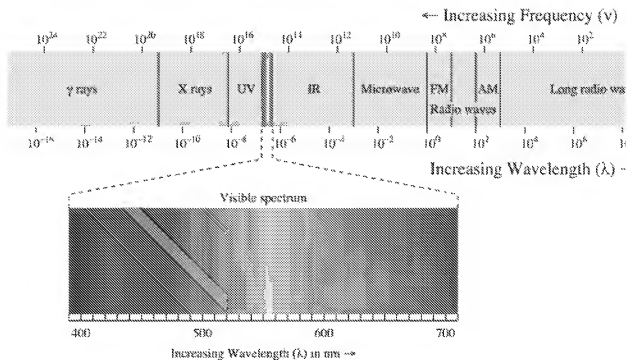
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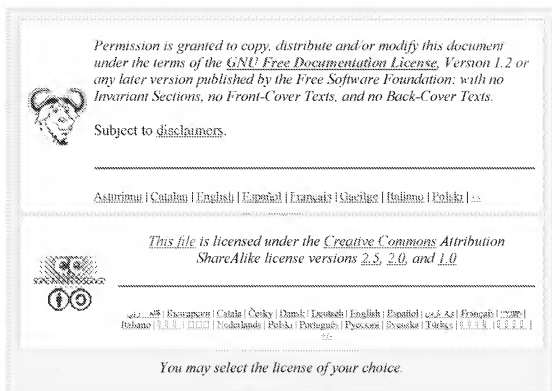
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- [Main Page](#)
- [Contents](#)
- [Featured content](#)
- [Current events](#)
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Ultraviolet

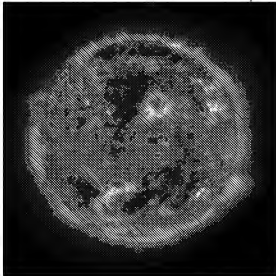
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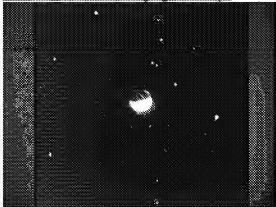
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"UV" redirects here. For other uses of UV, see [UV \(disambiguation\)](#).



[ⓘ] [False-color](#) image of the [solar corona](#) as seen in deep ultraviolet light at [17.1 nm](#) by the [Extreme ultraviolet Imaging Telescope](#) instrument aboard the [SOHO](#) spacecraft



[ⓘ] An ultraviolet photograph of the Earth taken from the Moon by [Apollo 16](#) astronauts.

Ultraviolet (UV) light is [electromagnetic radiation](#) with a [wavelength](#) shorter than that of [visible light](#), but longer than soft [X-rays](#). It is so named because the spectrum consists of

electromagnetic waves with frequencies higher than those that humans identify as the color violet (purple).

UV light is typically found as part of the radiation received by the Earth from the Sun. Most humans are aware of the effects of UV through the painful condition of sunburn. The UV spectrum has many other effects, including both beneficial and damaging changes to human health.

Contents

- [1 Discovery](#)
- [2 Origin of term](#)
- [3 Subtypes](#)
- [4 Black light](#)
- [5 Natural sources of UV](#)
- [6 Human Health Related Effects of UV Radiation](#)
 - [6.1 Beneficial effects](#)
 - [6.2 Harmful effects](#)
 - [6.2.1 Skin](#)
 - [6.2.2 Eye](#)
- [7 Degradation of polymers, pigments and dyes](#)
- [8 Blockers and absorbers](#)
- [9 Applications of UV](#)
 - [9.1 Black lights](#)
 - [9.2 Fluorescent lamps](#)
 - [9.3 Astronomy](#)
 - [9.4 Pest control](#)
 - [9.5 Spectrophotometry](#)
 - [9.6 Analyzing minerals](#)
 - [9.7 Chemical markers](#)
 - [9.8 Photochemotherapy](#)
 - [9.9 Phototherapy](#)
 - [9.10 Photolithography](#)
 - [9.11 Checking electrical insulation](#)
 - [9.12 Sterilization](#)
 - [9.13 Disinfecting drinking water](#)
 - [9.14 Food processing](#)
 - [9.15 Fire detection](#)
 - [9.16 Curing of inks, adhesives, varnishes and coatings](#)
 - [9.17 Deterring substance abuse in public places](#)
 - [9.18 Sun Tanning](#)
 - [9.19 Erasing EPROM modules](#)
 - [9.20 Preparing low surface energy polymers](#)
 - [9.21 Reading completely illegible papyruses](#)
- [10 Evolutionary significance](#)
- [11 See also](#)

- [12 Further reading](#)
- [13 References](#)

[edit] Discovery

The discovery of UV radiation was intimately associated with the observation that silver salts darken when exposed to sunlight. In 1801 the German physicist [Johann Wilhelm Ritter](#) made the hallmark observation that invisible rays just beyond the violet end of the visible spectrum were especially effective at darkening [silver chloride](#)-soaked paper. He called them "de-oxidizing rays" to emphasize their chemical [reactivity](#) and to distinguish them from "heat rays" at the other end of the visible spectrum. The simpler term "chemical rays" was adopted shortly thereafter, and it remained popular throughout the [19th century](#). The terms chemical and heat rays were eventually dropped in favor of ultraviolet and [infrared radiation](#), respectively.^[1]

[edit] Origin of term

The name means "beyond violet" (from [Latin](#) *ultra*, "beyond"), [violet](#) being the [color](#) of the shortest wavelengths of visible light. UV light has a shorter wavelength than that of violet light.

[edit] Subtypes

The part of the electromagnetic spectrum which ultraviolet light covers can be further subdivided in several different overlapping ways:

| Name | Abbreviation | Wavelength range in nanometers | Energy per photon |
|--|--------------|--|-------------------|
| Near | NUV | 400 nm - 200 nm | 3.10 - 6.20 eV |
| UVA, long wave, or black light | | 400 nm - 320 nm | 3.10 - 3.87 eV |
| UVB or medium wave | | 320 nm - 280 nm | 3.87 - 4.43 eV |
| UVC, short wave, or germicidal | | Below 280 nm | 4.43 - 6.20 eV |
| Far or vacuum | FUV, VUV | 200 nm - 10 nm | 6.20 - 124 eV |
| Extreme or deep | EUV, XUV | 31 nm - 1 nm | 40 - 1240 eV |

In [photolithography](#), in [laser](#) technology, etc., the term deep ultraviolet or DUV refers to wavelengths below 300 nm. "Vacuum UV" is so named because it is absorbed strongly by [air](#) and is used in vacuums.

See [1 E-7 m](#) for a list of objects of comparable sizes.

[edit] Black light

Main article: Black light

Ultraviolet is colloquially called black light, as it is invisible to the human cye. Some animals, including birds, reptiles, and insects such as bees, can see into the near ultraviolet. Many fruits, flowers, and seeds stand out more strongly from the background in ultraviolet wavelengths as compared to human color vision. Scorpions glow or take on a yellow to green color under UV illumination. Many birds have patterns in their plumage that are invisible at usual wavelengths but observable in ultraviolet, and the urine and other secretions of some animals, including dogs, cats, and human beings, is much easier to spot with ultraviolet.

[edit] Natural sources of UV

The Sun emits ultraviolet radiation in the UVA, UVB, and UVC bands, but because of absorption in the atmosphere's ozone layer, 99% of the ultraviolet radiation that reaches the Earth's surface is UVA. (Some of the UVB and UVC radiation is responsible for the generation of the ozone layer.)

Ordinary glass is partially transparent to UVA but is opaque to shorter wavelengths while Silica or quartz glass, depending on quality, can be transparent even to vacuum UV wavelengths. Ordinary window glass passes about 90% of the light above 350 nm, but blocks over 90% of the light below 300 nm.^{[2][3][4]}

The onset of vacuum UV, 200 nm, is defined by the fact that ordinary air is opaque below this wavelength. This opacity is due to the strong absorption of light of these wavelengths by oxygen in the air. Pure nitrogen (less than about 10 ppm oxygen) is transparent to wavelengths in the range of about 150–200 nm. This has wide practical significance now that semiconductor manufacturing processes are using wavelengths shorter than 200 nm. By working in oxygen-free gas, the equipment does not have to be built to withstand the pressure differences required to work in a vacuum. Some other scientific instruments, such as circular dichroism spectrometers, are also commonly nitrogen purged and operate in this spectral region.

Extreme UV is characterized by a transition in the physics of interaction with matter: wavelengths longer than about 30 nm interact mainly with the chemical valence electrons of matter, while wavelengths shorter than that interact mainly with inner shell electrons and nuclei. The long end of the EUV/XUV spectrum is set by a prominent He⁺ spectral line at 30.4nm. XUV is strongly absorbed by most known materials, but it is possible to synthesize multilayer optics that reflect up to about 50% of XUV radiation at normal incidence. This technology has been used to make telescopes for solar imaging; it was pioneered by the NIXT and MSSTA sounding rockets in the 1990s; (current examples are SOHO/EIT and TRACE) and for nanolithography (printing of traces and devices on microchips).

[edit] Human Health Related Effects of UV Radiation

[edit] Beneficial effects

A positive effect of UVB exposure is that it induces the production of vitamin D in the skin. It has been estimated that tens of thousands of premature deaths occur in the United States annually from a range of cancers due to vitamin D deficiency.^[5] Another effect of vitamin D deficiency is osteomalacia (the adult equivalent of rickets), which can result in bone pain, difficulty in weight bearing and sometimes fractures. Other studies show most people get adequate Vitamin D through food and incidental exposure.^[6]

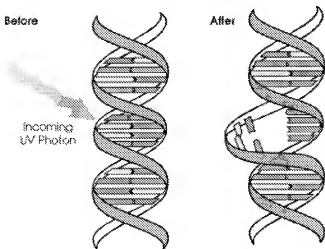
Many countries have fortified certain foods with Vitamin D to prevent deficiency. Eating fortified foods or taking a dietary supplement pill is usually preferred to UVB exposure, due to the increased risk of skin cancer from UV radiation.^[6]

Ultraviolet radiation has other medical applications, in the treatment of skin conditions such as psoriasis and vitiligo. UVA radiation can be used in conjunction with psoralens (PUVA treatment). UVB radiation is *rarely* used in conjunction with psoralens. In cases of psoriasis and vitiligo, UV light with wavelength of 311 nm is most effective.^[citation needed]

[edit] Harmful effects

In humans, prolonged exposure to solar UV radiation may result in acute and chronic health effects on the skin, eye, and immune system.^[7]

UVC rays are the highest energy, most dangerous type of ultraviolet light. Little attention has been given to UVC rays in the past since they are filtered out by the atmosphere. However, their use in equipment such as pond sterilization units may pose an exposure risk, if the lamp is switched on outside of its enclosed pond sterilization unit.



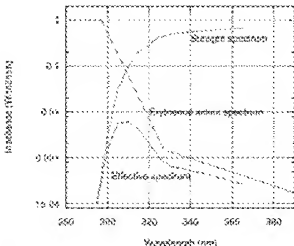
Ultraviolet photons harm the DNA molecules of living organisms in different ways. In one common damage event, adjacent Thymine bases bond with each other, instead of across the "ladder". This makes a bulge, and the distorted DNA molecule does not function properly.

[edit] Skin

Ultraviolet (UV) irradiation present in sunlight is an environmental human carcinogen. The toxic effects of UV from natural sunlight and therapeutic artificial lamps are a major concern for human health. The major acute effects of UV irradiation on normal human skin comprise sunburn inflammation, erythema, tanning, and local or systemic immunosuppression.

— Matsumura and Ananthaswamy, (2004)^[2]

UVA, UVB and UVC can all damage collagen fibers and thereby accelerate aging of the skin. Both UVA and UVB destroy vitamin A in skin which may cause further damage.^[19] In general, UVA is the least harmful, but can contribute to the aging of skin, DNA damage and possibly skin cancer. It penetrates deeply and does not cause sunburn. Because it does not cause reddening of the skin (erythema) it cannot be measured in the SPF testing. There is no good clinical measurement of the blocking of UVA radiation, but it is important that sunscreens block both UVA and UVB.



The reddening of the skin due to the action of sunlight depends both on the amount of sunlight as well as the sensitivity of the skin ("erythral action spectrum") over the UV spectrum.

UVB light can cause skin cancer. The radiation excites DNA molecules in skin cells, causing covalent bonds to form between adjacent thymine bases, producing thymidine

dimers. Thymidine dimers do not base pair normally, which can cause distortion of the DNA helix, stalled replication, gaps, and misincorporation. These can lead to mutations, which can result in cancerous growths. The mutagenicity of UV radiation can be easily observed in bacteria cultures. This cancer connection is one reason for concern about ozone depletion and the ozone hole. UVB causes some damage to collagen but at a very much slower rate than UVA.

As a defense against UV radiation, the body tans when exposed to moderate (depending on skin type) levels of radiation and UVA in particular triggers the release of the brown pigment melanin from melanocytes; while UVB mostly triggers de novo production. This tan helps to block UV penetration and prevent damage to the vulnerable skin tissues deeper down.

Suntan lotion, often referred to as "sun block" or "sunscreen", partly blocks UV and is widely available. Most of these products contain an SPF rating that describes the amount of protection given. This protection factor, however, applies only to UVB rays responsible for sunburn and not to UVA rays that penetrate more deeply into the skin and may also be responsible for causing cancer and wrinkles. Some sunscreen lotion now includes compounds such as titanium dioxide which helps protect against UVA rays. Other UVA blocking compounds found in sunscreen include zinc oxide and avobenzone. Cantaloupe extract, rich in the compound superoxide dismutase (SOD), can be bound with gliadin to form glisodin, an orally-effective protectant against UVB radiation. There are also naturally occurring compounds found in rainforest plants that have been known to protect the skin from UV radiation damage, such as the fern *Phlebodium aureum*.

What to look for in sunscreen

- UVB protection: Padimate O, Homosalate, Octisalate (octyl salicylate), Octinoxate (octyl methoxycinnamate)
- UVA protection: Avobenzone
- UVA/UVB protection: Octocrylene, titanium dioxide, zinc oxide, Mexoryl (ecamsule)

Another means to block UV is sun protective clothing. This is clothing that has a "UPF rating" that describes the protection given against both UVA and UVB.

[edit] Eye

High intensities of UVB light are hazardous to the eyes, and exposure can cause welder's flash (photokeratitis or arc eye) and may lead to cataracts, pterygium,^{[10][11]} and pinguecula formation.

Protective eyewear is beneficial to those who are working with or those who might be exposed to ultraviolet radiation, particularly short wave UV. Given that light may reach the eye from the sides, full coverage eye protection is usually warranted if there is an increased risk of exposure, as in high altitude mountaineering. Mountaineers are exposed

to higher than ordinary levels of UV radiation, both because there is less atmospheric filtering and because of reflection from snow and ice.

Ordinary, untreated eyeglasses give some protection. Most plastic lenses give more protection than glass lenses, because, as noted above, glass is transparent to UVA and the common acrylic plastic used for lenses is less so. Some plastic lens materials, such as polycarbonate, inherently block most UV. There are protective treatments available for eyeglass lenses that need it which will give better protection. But even a treatment that *completely* blocks UV will not protect the eye from light that arrives around the lens.

[edit] Degradation of polymers, pigments and dyes

Many polymers used in consumer products are degraded by UV light, and need addition of UV stabilizers to inhibit attack. Products include thermoplastics, such as polypropylene and polyethylene as well as speciality fibres like aramids. UV absorption leads to chain degradation and loss of strength. In addition, many pigments and dyes absorb UV and change colour, so paintings and textiles may need extra protection both from sunlight and fluorescent lamps.

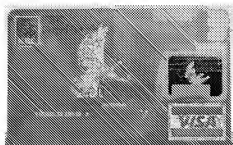
[edit] Blockers and absorbers

Ultraviolet Light Absorbers (UVAs) are molecules used in organic materials (polymers, paints, etc.) to absorb UV light in order to reduce the degradation (photo-oxidation) of a material. A number of different UVAs exist with different absorption properties. UVAs can disappear over time, so monitoring of UVA levels in weathered materials is necessary.

In sunscreen, ingredients which absorb UVA/UVB rays, such as avobenzone and octyl methoxycinnamate, are known as absorbers. They are contrasted with physical "blockers" of UV radiation such as titanium dioxide and zinc oxide. (See sunscreen for a more complete list.)

[edit] Applications of UV

[edit] Black lights





A bird appears on many Visa credit cards when held under a UV light source.

A black light is a lamp that emits long wave UV radiation and very little visible light. Fluorescent black lights are typically made in the same fashion as normal fluorescent lights except that only one phosphor is used and the normally clear glass envelope of the bulb is replaced by a deep bluish purple glass called Wood's glass.

To help thwart counterfeiters, sensitive documents (e.g. credit cards, driver's licenses, passports) may also include a UV watermark that can only be seen when viewed under a UV-emitting light. Passports issued by most countries usually contain UV sensitive inks and security threads. Visa stamps and stickers on passports of visitors contain large and detailed seals invisible to the naked eye under normal lights, but strongly visible under UV illumination. Passports issued by many nations have UV sensitive watermarks on all pages of the passport. Currencies of various countries' banknotes have an image, as well as many multicolored fibers, that are visible only under ultraviolet light.

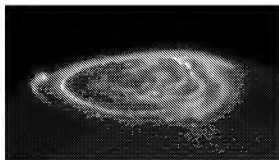
[edit] Fluorescent lamps

Fluorescent lamps produce UV radiation by ionising low-pressure mercury vapour. A phosphorescent coating on the inside of the tubes absorbs the UV and converts it to visible light.

The main mercury emission wavelength is in the UVC range. Unshielded exposure of the skin or eyes to mercury arc lamps that do not have a conversion phosphor is quite dangerous.

The light from a mercury lamp is predominantly at discrete wavelengths. Other practical UV sources with more continuous emission spectra include xenon arc lamps (commonly used as sunlight simulators), deuterium arc lamps, mercury-xenon arc lamps, metal-halide arc lamps, and tungsten-halogen incandescent lamps.

[edit] Astronomy



Aurora at Jupiter's north pole as seen in ultraviolet light by the Hubble Space Telescope.

In astronomy, very hot objects preferentially emit UV radiation (see Wien's law). Because the ozone layer blocks many UV frequencies from reaching telescopes on the surface of the Earth, most UV observations are made from space. (See UV astronomy, space observatory.)

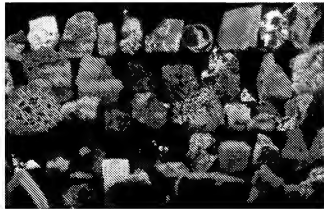
[edit] Pest control

Ultraviolet traps are used to eliminate various small flying insects. They are attracted to the UV light, and are killed using an electric shock, or trapped once they come into contact with the device.

[edit] Spectrophotometry

UV/VIS spectroscopy is widely used as a technique in chemistry, to analyze chemical structure, most notably conjugated systems. UV radiation is often used in visible spectrophotometry to determine the existence of fluorescence in a given sample.

[edit] Analyzing minerals



⁵²
A collection of mineral samples brilliantly fluorescing at various wavelengths as seen while being irradiated by UV light.

Ultraviolet lamps are also used in analyzing minerals, gems, and in other detective work including authentication of various collectibles. Materials may look the same under visible light, but fluoresce to different degrees under ultraviolet light; or may fluoresce differently under short wave ultraviolet versus long wave ultraviolet.

[edit] Chemical markers

UV fluorescent dyes are used in many applications (for example, biochemistry and forensics). The Green Fluorescent Protein (GFP) is often used in genetics as a marker. Many substances, such as proteins, have significant light absorption bands in the

ultraviolet that are of use and interest in biochemistry and related fields. UV-capable spectrophotometers are common in such laboratories.

[[edit](#)] Photochemotherapy

Exposure to UVA light while the skin is hyper-photosensitive by taking [psoralens](#) is an effective treatment for [psoriasis](#) called [PUVA](#). Due to [psoralens](#) potentially causing damage to the [liver](#), [PUVA](#) may only be used a limited number of times over a patient's lifetime.

[[edit](#)] Phototherapy

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Exposure to UVB light, particularly the 310nm narrowband UVB range, is an effective long-term treatment for many skin conditions like [psoriasis](#), [vitiligo](#), [eczema](#), and many others. UVB phototherapy does not require additional medications or topical preparations for the therapeutic benefit; only the light exposure is needed. However, phototherapy can be effective when used in conjunction with certain topical treatments such as anthralin, coal tar, and Vitamin A and D derivatives, or systemic treatments such as methotrexate and [soriatane](#).^{[\[12\]](#)}

Typical treatment regimes involve short exposure to UVB rays 3 to 5 times a week at a hospital or clinic, and for the best results, up to 30 or more sessions may be required.

Side effects may include itching and redness of the skin due to UVB exposure, and possibly sunburn, if patients do not minimize exposure to natural UV rays during treatment days.

[[edit](#)] Photolithography

Ultraviolet radiation is used for very fine resolution [photolithography](#), a procedure where a chemical known as a photoresist is exposed to UV radiation which has passed through a mask. The light allows chemical reactions to take place in the photoresist, and after development (a step that either removes the exposed or unexposed photoresist), a geometric pattern which is determined by the mask remains on the sample. Further steps may then be taken to "etch" away parts of the sample with no photoresist remaining.

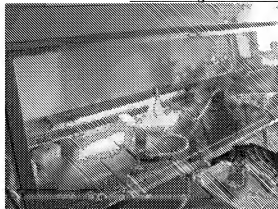
UV radiation is used extensively in the electronics industry because photolithography is used in the manufacture of semiconductors, integrated circuit components^[13] and printed circuit boards.

[edit] Checking electrical insulation

A new application of UV is to detect corona discharge (often simply called "corona") on electrical apparatus. Degradation of insulation of electrical apparatus or pollution causes corona, wherein a strong electric field ionizes the air and excites nitrogen molecules, causing the emission of ultraviolet radiation. The corona degrades the insulation level of the apparatus. Corona produces ozone and to a lesser extent nitrogen oxide which may subsequently react with water in the air to form nitrous acid and nitric acid vapour in the surrounding air.^[14]

[edit] Sterilization

Main article: Ultraviolet germicidal irradiation



A low pressure mercury vapor discharge tube floods the inside of a hood with shortwave UV light when not in use, sterilizing microbiological contaminants from irradiated surfaces.

Ultraviolet lamps are used to sterilize workspaces and tools used in biology laboratories and medical facilities. Commercially-available low pressure mercury-vapor lamps emit about 86% of their light at 254 nanometers (nm) which coincides very well with one of the two peaks of the germicidal effectiveness curve (i.e., effectiveness for UV absorption by DNA). One of these peaks is at about 265 nm and the other is at about 185 nm. Although 185 nm is better absorbed by DNA, the quartz glass used in commercially-available lamps, as well as environmental media such as water, are more opaque to 185 nm than 254 nm (C. von Sonntag et al., 1992). UV light at these germicidal wavelengths causes adjacent thymine molecules on DNA to dimerize, if enough of these defects accumulate on a microorganism's DNA its replication is inhibited, thereby rendering it harmless (even though the organism may not be killed outright). However, since

microorganisms can be shielded from ultraviolet light in small cracks and other shaded areas, these lamps are used only as a supplement to other sterilization techniques.

[edit] Disinfecting drinking water

UV radiation can be an effective viricide and bactericide. Disinfection using UV radiation is more commonly used in wastewater treatment applications but is finding increased usage in drinking water treatment. A process named SODIS [1] has been extensively researched in Switzerland and has proven ideal to treat small quantities of water. Contaminated water is poured into transparent plastic bottles and exposed to full sunlight for six hours. The sunlight treats the contaminated water through two synergetic mechanisms: Radiation in the spectrum of UV-A (wavelength 320-400nm) and increased water temperature. If the water temperatures rises above 50°C, the disinfection process is three times faster. It used to be thought that UV disinfection was more effective for bacteria and viruses, which have more exposed genetic material, than for larger pathogens which have outer coatings or that form cyst states (e.g., Giardia) that shield their DNA from the UV light. However, it was recently discovered that ultraviolet radiation can be somewhat effective for treating the microorganism Cryptosporidium. The findings resulted in two US patents and the use of UV radiation as a viable method to treat drinking water. Giardia in turn has been shown to be very susceptible to UV-C when the tests were based on infectivity rather than excystation.^[13] It has been found that protists are able to survive high UV-C doses but are sterilized at low doses.

[edit] Food processing

As consumer demand for fresh and "fresh like" food products increases, the demand for nonthermal methods of food processing is likewise on the rise. In addition, public awareness regarding the dangers of food poisoning is also raising demand for improved food processing methods. Ultraviolet radiation is used in several food processes to remove unwanted microorganisms. UV light can be used to pasteurize fruit juices by flowing the juice over a high intensity ultraviolet light source. The effectiveness of such a process depends on the UV absorbance of the juice (see Beer's law).

[edit] Fire detection

Ultraviolet detectors generally use either a solid-state device, such as one based on silicon carbide or aluminium nitride, or a gas-filled tube as the sensing element. UV detectors which are sensitive to UV light in any part of the spectrum respond to irradiation by sunlight and artificial light. A burning hydrogen flame, for instance, radiates strongly in the 185 to 260 nanometer range and only very weakly in the IR region, while a coal fire emits very weakly in the UV band yet very strongly at IR wavelengths; thus a fire detector which operates using both UV and IR detectors is more reliable than one with a UV detector alone. Virtually all fires emit some radiation in the UVB band, while the Sun's radiation at this band is absorbed by the Earth's atmosphere. The result is that the UV detector is "solar blind", meaning it will not cause an alarm in response to radiation from the Sun, so it can easily be used both indoors and outdoors.

UV detectors are sensitive to most fires, including hydrocarbons, metals, sulfur, hydrogen, hydrazine, and ammonia. Arc welding, electrical arcs, lightning, X-rays used in nondestructive metal testing equipment (though this is highly unlikely), and radioactive materials can produce levels that will activate a UV detection system. The presence of UV-absorbing gases and vapors will attenuate the UV radiation from a fire, adversely affecting the ability of the detector to detect flames. Likewise, the presence of an oil mist in the air or an oil film on the detector window will have the same effect.

[edit] Curing of inks, adhesives, varnishes and coatings

Certain inks, coatings and adhesives are formulated with photoinitiators and resins. When exposed to the correct energy and irradiance in the required band of UV light, polymerization occurs, and so the adhesives harden or cure. Usually, this reaction is very quick, a matter of a few seconds. Applications include glass and plastic bonding, optical fiber coatings, the coating of flooring, UV Coating and paper finishes in offset printing, and dental fillings.

An industry has developed around the manufacture of UV lamps sourced for UV curing applications. Fast processes such as flexo or offset printing require high intensity light focussed via reflectors onto a moving substrate and medium and high pressure Hg (mercury) or Fe (iron) based bulbs are used which can be energised with electric arc or microwaves. Lower power fluorescent lamps can be used for static applications and in some cases, small high pressure lamps can have light focussed and transmitted to the work area via liquid filled or fibre optic light guides.

Radtech is a trade association dedicated to the promotion of this technology.

[edit] Deterrent substance abuse in public places

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UV lights have been installed in some parts of the world in public restrooms, and on public transport, for the purpose of deterring substance abuse. The blue color of these lights, combined with the fluorescence of the skin, make it harder for intravenous drug users to find a vein.^[16] The efficacy of these lights for that purpose has been questioned, with some suggesting that drug users simply find a vein outside the public restroom and mark the spot with a marker for accessibility when inside the restroom. There is currently no published evidence supporting the idea of a deterrent effect.

[edit] Sun Tanning

Sun tanning describes a darkening of the skin (especially of fair-skinned individuals) in a natural physiological response stimulated by exposure to ultraviolet radiation from

sunshine (or a sunbed). With excess exposure to the sun, a suntanned area can also develop sunburn.

[edit] Erasing EPROM modules

Some EPROM (electronically programmable read-only memory) modules are erased by exposure to UV radiation. These modules often have a transparent glass (quartz) window on the top of the chip that allows the UV radiation in. These have been largely superseded by EEPROM and flash memory chips in most devices.

[edit] Preparing low surface energy polymers

UV radiation is useful in preparing low surface energy polymers for adhesives. Polymers exposed to UV light will oxidize thus raising the surface energy of the polymer. Once the surface energy of the polymer has been raised, the bond between the adhesive and the polymer will not be smaller.

[edit] Reading completely illegible papyruses

Using multi-spectral imaging it is possible to read illegible papyruses, such as the burned papyruses of the Villa of the Papyri or of Oxyrhynchus. The technique involves taking pictures of the illegible papyruses using different filters in the infrared or ultraviolet range, finely tuned to capture certain wavelengths of light. Thus, the optimum spectral portion can be found for distinguishing ink from paper on the papyrus surface.

[edit] Evolutionary significance

Evolution of early reproductive proteins and enzymes is attributed in modern models of evolutionary theory to ultraviolet light. Ultraviolet light causes thymine base pairs next to each other in genetic sequences to bond together into thymine dimers, a disruption in the strand which reproductive enzymes cannot copy (see picture above). This leads to frameshifting during genetic replication and protein synthesis, usually killing the organism. As early prokaryotes began to approach the surface of the ancient oceans, before the protective ozone layer had formed, blocking out most wavelengths of UV light, they almost invariably died out. The few that survived had developed enzymes which verified the genetic material and broke up thymine dimer bonds, known as excision repair enzymes. Many enzymes and proteins involved in modern mitosis and meiosis are extremely similar to excision repair enzymes, and are believed to be evolved modifications of the enzymes originally used to overcome UV light.^[17]

[edit] See also

- UV index
- High energy visible light
- Sun tanning

- Black light
- Wood's lamp
- UV Stabilizers in plastics
- Ultraviolet photography

[edit] Further reading



Look up *Ultraviolet* in
Wiktionary, the free dictionary.

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- [Current events](#)
- [Random article](#)

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